APPLIED PHYSICAL DIAGNOSIS

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Preface to Second Edition

The gratifying reception accorded the first edition has placed a heavy responsibility upon the editor and contributors to keep the book in line with current trends in teaching as well as with clinical practice. The place of physical diagnosis in the medical school curriculum continues to undergo searching analysis. Modern teaching now calls for greater correlation of bedside observations and the interpretation of accessory diagnostic technics, especially roentgenography and laboratory diagnosis. In no way does this concept detract from the importance of a painstaking medical history and thorough physical examination, but it does make for more intelligent selection of additional diagnostic procedures

To bring this edition abreast of the rapid progress in medical diagnosis, several major changes have been necessitated. It must be emphasized that the scope of the book has been aimed towards the development of the methods of medical diagnosis which will be found useful to the general practitioner as well as to the student. All sections of the book have been subjected to careful scrutiny to determine their relative importance to clinical practice. Inasmuch as no one knows just what a general practitioner should or should not know, the selection of material to be added or deleted has been at best an arbitrary one, for which the editor accepts full responsibility. The regional method of presentation employed in the first edition has been retained. The sections on the examinations of the eye, the abdomen and electrocardiographic interpretation have been completely rewritten. New chapters include one on the bedside diagnosis of blood diseases (recognizing the blood as an organ) by Drs. Edward D. Thomas and Clement A. Finch, one on medical diagnosis in the aged by Dr. Ernst P. Boas, and one on the physical examination of the psychiatric patient by Dr. Melvin W. Thorner.

With deep regret, the editor reports the death of two contributors to the first edition: Drs. John H. Musser and Hugh Auchincloss. Dr. Auchincloss was able nearly to complete the revision of his chapter before his untimely death; the revision was completed by his colleagues, Drs. Cushman Haagensen and Virginia Frantz, and his son, Dr. Hugh Auchincloss, Jr.

Acknowledgments in a work of this type are so many as to be beyond the space allotments. To the contributors who continue to labor faithfully and enthusiastically over the revisions, to the many teachers and physicians from all parts of the world who have offered criticisms and suggestions, and to the medical students who are, in the final analysis, the most severe critics, the editor expresses his deepest appreciation. Special appreciation is likewise due the W. B Saunders Company for their painstaking attention to all details concerned with the publication of this volume. Finally, the editor wishes to thank his wife, Gwendolen Williams Pullen, for her patience and encouragement throughout the many months of preparation of this revision.

June, 1950 ROSCOE L. PULLEN
New Orleans, Louisiana

Preface to First Edition

To present to the profession another textbook of medical diagnosis demands an unswerving conviction that such a text will fulfill an apparent need. First and foremost, one cannot stress too strongly that examination of the patient is the keystone to diagnosis, and that errors in diagnosis result more frequently from errors of omission than from those of commission. Many of the diseases which affect man are protean in character. This presumes that attention will be directed to a thorough examination of the *whole* body, rather than only to certain systems such as the heart and lungs.

Secondly the scope of medical diagnosis has undergone sweeping changes No longer is the subject considered apart from disease; its direct relationship to altered body states, whether physiologic or anatomic, must be understood. To seek an explanation of the various symptoms and signs of disease processes is accordingly the primary objective of medical diagnosis. Medical diagnosis *per se* differs from medicine and surgery in that it emphasizes diagnostic methods utilized in the determination of the expressions of disease states; it does not establish an etiologic diagnosis except in those instances wherein the anatomic deviations revealed by the examiner are of such character as to permit an insight into the causation. The methods of diagnosis have been expanded to incorporate all means which the clinician must summon to his command in the examination of the patient. This includes the history, physical examination, and the utilization of various accessory procedures in the form of endoscopic, roentgenographic, fluoroscopic, and histologic studies found helpful in the interpretation of various physical phenomena at the bedside.

Such a concept has effected drastic alterations in our teaching of medical diagnosis, especially physical diagnosis, for physical diagnosis is part and parcel of medical diagnosis Formerly, physical diagnosis had been relegated to a minor position in the curriculum of many medical schools, and was generally taught by the medical departments. As a result, the student focused undue attention on various parts of the body, especially the examination of the chest, which are acknowledged to lie within the field of the internist. It is appreciated now that the development of the ability to examine all parts of the body is the primary responsibility of every department, and that the development of the art of medical diagnosis begins early in the clinical years of medical school and progresses thereafter for each and every day that the physician practices. On the acquisition and perfection of this art will depend, to no inconsiderable degree, the ability of the clinician as a diagnostician and therapist alike. Medical diagnosis, with the principles of physical diagnosis, therefore marks one of the major subjects in the medical school curriculum to be taught and reëmphasized until the student becomes proficient in the art.

In this volume we have attempted to review the subject of medical diagnosis in the present light. The contents and arrangement of the first portion

of the book conform to our concept of a logical, orderly procedure for examination of the patient as a whole. The second portion of the book has been incorporated with the humble hope that the subject matter discussed therein will enhance considerably the interpretation of disease processes revealed by the examiner, and meet the needs of the busy practitioner for special consideration of his more common problems. The presentation and style from chapter to chapter will vary within the legitimate limits afforded by the part of the body under discussion The dominant theme throughout all the chapters has been to portray the methods of diagnosis and their interpretation applicable to each individual system or region of the body.

The editor wishes to express, though he feels he can do so inadequately, his appreciation to all those who aided him in the preparation of this book. To all the busy contributors who have given so generously of their time and efforts in the preparation of this book, the editor expresses his sincere thanks and gratitude The inspiration and kindly counsel of Dr. John H. Musser has been of the greatest importance in making this book possible. Dr. Alton Ochsner has rendered timely advice concerning the surgical sections of the book. Dr. Merrill Moore has offered invaluable suggestions concerning the psychiatric section. Dr. T. Lyle Hazlett, Medical Director of the Westinghouse Electric and Manufacturing Company, has kindly criticized the manuscript from the point of view of occupational problems. Drs Francis Bayard Carter, Stanley Cobb, E C. Hamblen, Edgar Hull, Richard S Lyman, Robert A. Kehoe, Edward A. Oliver, and Robert S. Schwab have given valuable advice and assistance

For invaluable advice in the preparation of the manuscript, the editor is also grateful to his former associates, Captain John D Welch and Captain James A Wilson of the Medical Corps, Army of the United States; and is deeply indebted to Miss Vera Morel of the Department of Medical Illustration, Tulane University of Louisiana School of Medicine, for her many generous contributions to the illustrations of the book. In addition, special appreciation is rendered to Miss Lucille Cassell of Northwestern University Medical School, Mr. William Branks Stewart of Louisiana State University School of Medicine, Miss Mary Ellen Frölich of New Orleans, Mr. Elon H Clark of Duke University School of Medicine, Miss Elizabeth H Broedel of Cornell University Medical College, and to many others for their courteous assistance. Much secretarial aid has been given by Miss Tilly Bert Rivet and Mrs. Gusse Patten And the editor's wife, Gwendolen Williams Pullen, has inspired him and granted much time and assistance throughout the many months of the book's preparation

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By Roscoe L. Pullen

I

THE MEDICAL HISTORY

It can be accepted generally that a person consults a physician whenever anything interferes with his work or comfort. It matters not to the patient that the symptoms may be functional or organic in origin; what matters is that he has sufficient complaints to seek medical aid. It cannot be stressed too strongly, therefore, that the physician should receive the patient's history with a kindly, sympathetic attitude, paying equal attention to the ailments of the mind and to those of the body until each can be assigned to its proper perspective in the disentanglement of the apparent disabilities.

Furthermore, the symptoms of disease, representing, as they do, the subjective sensations or acts of altered function of body processes, are oftentimes the earliest clues to anatomic deviations to be subsequently revealed by the examiner. In the majority of instances, symptoms antedate the gross pathologic alterations of disease and as such present the earliest manifestations of disease processes, a view advanced by Mackenzie. Therein, too, lies our greatest hope of therapeutic success, for the functional alterations of disease are generally more amenable to therapy than the irretrievable changes revealed so strikingly on the postmortem table. In many cases, symptoms are the only data discernible in the examination of the patient and must, therefore, be accepted tentatively as a diagnosis, although it is difficult to conceive of pain, for example angina pectoris, as a clinical entity. For the time being, such a diagnosis will stand as an admission of our ignorance of the underlying defects. Moreover, it must be accepted at the very start that symptoms arise not only from anatomic derangements but from physiologic disturbances, and that often we must turn to the laboratory for explanation. Inasmuch as symptoms can be appreciated only by the patient, the character of the complaints will be widely divergent, depending upon the psychic coloring of the patient, individual threshold to discomfort and a host of other factors.

From such a discussion, it is obvious that the medical history should not be skimmed over too lightly, for it usually establishes the baseline from which further diagnostic and therapeutic procedures may be initiated Furthermore, it will be acknowledged that the history taking itself is something of an art acquired by experience, deep-seated knowledge of physiologic and anatomic deviations of disease, and profound understanding of human frailties.

In the following paragraphs, we shall attempt to clarify the salient features of the medical history.

OPENING STATEMENT

In addition to the vital statistics of the patient, it is usually expeditious to note briefly the complaints of the moment and their duration. Such a factual statement contains not only the reason for which the patient seeks professional services but summarizes succinctly the diagnostic approach. Brevity is its keyword, as well as its value and its fault. We employ a symbolic figure *para 0-0-0* to describe the reproductive status of the female patient. Such a term is easy to interpret and infinitely descriptive: *para 0-0-0*, for example, means that the woman has had no pregnancies, no abortions or miscarriages, and no living children (*p* for pregnancies, *a* for abortions or miscarriages, *r-a* for children remaining alive). To illustrate, the opening statement may read as follows: "This 26 year old, white, married female, para 1-0-1, presents herself for an evaluation of pain in the right lower quadrant, nausea and vomiting of six hours duration."

PRESENT ILLNESS

Whether or not the present illness should be recorded next in the order of the history is a much debated point. It is certainly true that most patients prefer to discuss their chief complaints immediately upon consultation with the physician rather than delay the presentation of the reasons why they sought medical aid. Moreover, the exigencies of practice, especially in acute or emergency cases, often demand immediate investigation of the problem at hand. Again, the development of the present illness permits the doctor to gain the patient's confidence so that, after a time, detailed information of intimate subjects may be freely obtained; this is of especial importance in functional disturbances. By the same token, the physician is privileged to observe his patient during the narration of the present illness and to evaluate the patient's emotional and mental constitution—a consideration of far reaching clinical significance—as well as the physical status

On the other hand, the garrulous patient may burden the physician with a rambling mass of irrelevant facts which are difficult to organize; in such instances, the physician may have recourse to direct questioning, with particular reference to a painstaking review of systems. Again, the examiner may prefer to reconstruct the patient's description of his present illness later in pertinent, logical form using medical terminology, thus shifting this portion of the medical history to the end The preferable method of recording the present illness cannot be dictated; the choice will depend upon the individual case and the attending physician.

Theoretically, the description of the present illness should represent a chronologic account of the immediate symptoms of the patient as related in his own words, for leading questions on the part of the examiner often induce the patient to give the answers he believes he is expected to give. On the other hand, this is not entirely practical from the clinical viewpoint, for patients with limited vocabulary not only find it difficult to describe their various symptoms but are apt to have forgotten previous complaints which will be recalled upon interrogation by the physician Again, some patients possess a preconceived idea of the nature of their illness which prompts them to neglect certain symptoms in favor of others thought to blend more harmoniously with their disability. Herein lies the art of obtaining a good history; herein lies, too, the very essence of diagnosis for an intelligently developed history of the present illness should suggest certain entities which

can be enlarged or discarded as the occasion demands. One patient will need to be guided lest he stray from the trend of investigation; another will need persistent direct questioning until the story has been evoked. To facilitate organization and later reconstruction, the examiner will find it wise not to write the description of the present illness in full at the moment but to jot down short notes which can be enlarged and assembled in proper order as the history progresses.

With reference to the onset, it cannot be stressed too strongly that accurate dates be employed in recording the onset of the present conditions, and, if necessary, the developments hour by hour, avoiding generalities as days of the week or time intervals measured broadly by weeks or months. This is facilitated by a determination of the time when the patient last felt well.

Since most symptoms, e. g., pain, dyspnea, nausea, vomiting, headache, may be produced by widely divergent causes, the physician should learn as much about each symptom as possible: onset, location, quality, intensity, possible radiation, distribution, persistency or intermittency, duration, relationship to other complaints or certain bodily functions, such as eating, bowel movements, micturition, sleeping, working, menses, and any measures which may grant relief.

FAMILY HISTORY

Heredity. Inasmuch as the physician of today rarely has the intimate knowledge of the immediate relatives and ancestors of the patient that our predecessors possessed, he is forced to rely upon the patient's somewhat inaccurate picture of the family tree. That the constitutional and hereditary factors in the etiology of various diseases cannot be overlooked has become increasingly important in recent years as a result of the studies of various degenerative conditions. Not only do we inherit such characters as color, shape, size, vigor, fertility, longevity, and the like, but the profession recognizes that a large number of diseases, many of them rare, have genetic representation in the chromosomes (Boyd). Among these are allergic disorders; degenerative vascular diseases, as arteriosclerosis, coronary artery disease, angina pectoris, hypertension, nephritis, and migraine; cancer; blood dyscrasias, as hemophilia, pernicious anemia and sickle cell anemia; metabolic disorders, as diabetes mellitus, gout, obesity, lipoid storage diseases (as Gaucher's disease, Niemann-Pick disease), abnormal glycogen storage (von Gierke's disease), alkaptonuria and cystinuria; skeletal malformations of various types; dermatologic diseases, chief of which are baldness, multiple neurofibromata (von Recklinghausen's disease) and xeroderma pigmentosum (Kaposi's disease); a host of mental and nervous diseases, as schizophrenia, Huntington's chorea, feeblemindedness, amaurotic family idiocy and Mongolian idiocy, and the various degenerative lesions within the central nervous system; and diverse ophthalmologic conditions.

The occurrence of such conditions may not appear within the generation under observation but may lie dormant, appear in earlier ancestors or spasmodically along the family tree, or affect associated phenomena which can be explained only by careful inquiry into the family lineage until the aforementioned pathologic entity has been revealed.

Environment. The family history not only discloses the hereditary defects mentioned above but also affords considerable insight into the environmental factors underlying disease and the possibilities of direct

infection, as tuberculosis and syphilis. Although we know that the Jews, Chinese, Negroes, Hindus, Nordics and other races possess inherent susceptibilities to certain diseases, we are not certain whether these represent hereditary or environmental factors—or both. Not only do endemic infections, geography, and the established standards of living in a given area profoundly affect disease, but climate, as shown by Mills, is of considerable moment. The decreased vigor of the tropical dweller resulting from the influences of heat and humidity render him less vulnerable to vascular changes engendered by the increased tempo of living in the temperate zones, such as coronary artery disease, angina pectoris, rheumatic fever, hypertension, and nephritis. Similarly, he is less apt to develop other diseases as diabetes mellitus, pernicious anemia, toxic goiter, leukemia and Addison's disease. On the other hand, he is far more susceptible to parasitic infections and avitaminoses, especially vitamin B deficiency.

DEVELOPMENTAL HISTORY

Of especial significance in the evaluation of growth and development of the patient is a careful investigation into the developmental history. As stressed by Hamblen, this considers the growth and maturation of the patient according to physiologic epochs: the natal period; infancy; juvenility; adolescence; maturity, including menstrual, marital and obstetric facts; climacteric; and senescence. All data pertinent to these periods should be ascertained, the trend of the investigation being guided by the subject under consideration. For example, in an adult whose complaint is obesity, it is pertinent to know whether it began at some particular phase of childhood or whether it was related to a recent pregnancy. Clinically, the developmental history finds its greatest value in the pediatric, endocrine, metabolic and gynecologic histories.

Menstrual History. One subject which should never be neglected in the female patient is the menstrual history—onset of menarche, date of last period, interval between periods, number of days of flow, number of pads required daily, presence of menstrual molimina as dysmenorrhea, premenstrual tension, cyclomastopathy, and date and character of the menopause if such has occurred.

Terminology. In the past, a confusing and ponderous terminology concerning various menstrual irregularities has been employed. These terms are of relatively little value for they indicate nothing about the type of endometrium from which the bleeding occurs. The important fact in a menstrual irregularity is to determine whether it is associated with a progestational or estrogenic type of endometrium, these histologic studies being made possible by the technic of endometrial biopsy taken at the onset of a bleeding episode.

It is appropriate, therefore, to describe menstrual irregularities in simple terms and, when the endometrial background has been determined, to classify them according to the plan adopted by Hamblen:

1. Progestational or menstrual bleeding.
   a, Normal menstruation; *b,* infrequent menstruation; *c,* too frequent bleeding; or *d,* prolonged bleeding.
2. Estrogenic or interval bleeding
   a, Cyclic; *b,* infrequent; *c,* too frequent; or *d,* prolonged acyclic.
3. Nonoccurrence of bleeding (amenorrhea).

Marital History. Because of its many important implications, the marital history is considered separately. This includes pertinent data concerning the health of the mate; number of children; miscarriages and pregnancies; infections within the family, as tuberculosis, syphilis, and gonorrhea; dietary factors and living conditions; domestic and sexual happiness; and any apparent difficulties in the marital union.

OCCUPATIONAL HISTORY

Although for many years it has been recognized generally that many forms of occupation, especially the trades, are associated with considerable hazard, it should not be overlooked that the occupation of an individual in other walks of life may be related directly or indirectly to his complaints.There are a variety of factors in the occupation of the individual which may influence the present illness: exposure to various irritating substances; contact with domestic animals or diverse animal products, especially food products; the energy requirements of the work, whether active or sedentary; existence of such detrimental environmental conditions as climate, ventilation, lighting, heating, noise and unhygienic surroundings; adjustment factors both emotionally and physically to the innate demands of the work, including attitude towards nature of the job itself, superior officers, fellow employees, recreational facilities, and opportunities for advancement or promotion. In many instances, the occupation of the moment may be an adaptation to the patient's present health. More specifically, we may tabulate a rather large group of clinical diseases ascribable to occupational contacts (Sutton):

Industrial Diseases. These are receiving increasing attention from the medical profession, so much so that a special branch for the problems of industrial medicine has been established. *Pneumoconiosis*, or fibrosis of the lung parenchyma due to the inhalation of organic dusts, is a definite hazard of operators of tool-grinding machines such as those employed by miners, stonecutters, potters, glass polishers, file cutters, and the like, not to mention the various dusts derived from asbestos, cottons, woolens, bagasse (sugar cane), maple logs, etc. *Lead poisoning* may be acquired by inhalation, ingestion or absorption through the skin of lead dust or fumes, the chief incidence of such occurring among workers in lead mines, smelters, storage battery industry, paint manufacture and distribution, glass and pottery manufacture, plumbing and dye industries. *Mercurial poisoning* may develop in workers engaged in the fur trades, in the hat-making industries and in the manufacture of mirrors. *Arsenical poisoning* may be found in wallpaper workers, furriers, or artificial flower makers, not overlooking those handling the various pest poisons employed in agricultural pursuits. *Phosphorus poisoning* may appear in workers in the match industry. The so-called "brass-founders' ague" in workers in brass foundries means *chromium* and *zinc poisoning*. *Caisson disease*, or the "bends," is the dread entity to which those working in compressed air, as tunnel workers and divers, may be subject as a result of too rapid decompression *Pulmonary emphysema* may develop in glass blowers and musicians playing wind instruments *Nystagmus* is occasionally seen in miners. Diverse *effects of radiation energy* may appear among those working in pitchblende mines. The hazards of personnel handling radioactive isotopes or other fission products are too specialized to warrant discussion. Some

forms of bladder tumors are ascribable to ***beta-naphthylamine poisoning***. ***Contact dermatitis*** is a frequent result of exposure to diverse organic materials used in industry. ***Heat exhaustion*** may arise in those working in great environmental heat. ***Occupational neuroses*** (e. g., writer's cramp) may appear as cramps of muscles employed in constant repetition of some task. The role of trauma is apparent.

Infectious Diseases. According to Meyer, at least seventy-five diseases of domestic and wild animals may adversely affect man's health and welfare. *His article tabulates the diseases of man which find a reservoir in the animal* kingdom. The list is so impressive that a thorough epidemiologic slant becomes essential to the medical history of patients with infectious diseases. *This presupposes not only knowledge of the transmission of these diseases* but also comprehension of their clinical courses (Pullen). In general, transmission to man takes place chiefly by the cutaneous, the alimentary or the mucosal aerogenic routes, transfer being effected by contact with animals or their products or by intermediate vectors. Inasmuch as certain infectious diseases appear commonly among farmers, butchers, packing house employees, hunters, woodsmen, trappers, as well as the consumers of animal products, the occupational history may suggest both the diagnosis and the epidemiology of many infections These include undulant fever acquired from cattle, goats, hogs, horses and possibly dogs; tuberculosis from cattle and birds; salmonella infections from dogs, cats, cattle, hogs, sheep, barnyard fowls, rats and mice; anthrax from cattle, sheep, hogs, minks and possibly other animals; glanders from horses and mules; tularemia from rabbits; rabies from dogs and other carnivores; psittacosis from parrots, parakeets, pigeons, chickens, ducks, canaries, and psittacine birds; leptospirosis (Weil's disease) from rats, mice, dogs, cats, pigs, horses, foxes, and cattle; actinomycosis from cattle and cereal grains—to mention but a few. The geographic location of the occupation suggests certain clinical entities, such as coccidioidomycosis in the San Joaquin Valley of California, Rocky Mountain spotted fever in the Bitter Root Valley of Montana, and the like. Although indirectly related, the role of the environmental factors of occupation (as climate, ventilation, heat, unhygienic surroundings and the like) in the perpetuation and transmission of various infectious diseases, such as the *infections of the upper respiratory tract, is readily* appreciated.

SOCIAL HISTORY

This concerns those facts in the patient's background which may have considerable bearing upon the present illness At the outset, it must be acknowledged that functional distresses are common indeed and that differentiation of the resulting symptom complexes from organic disease is often fraught with considerable difficulty. Moreover, the course of organic disease is guided frequently by the emotional adjustment of the patient; one need only recall that attacks of angina pectoris may be precipitated by excitement in order to realize the validity of this. Granting that the social history may be sketched briefly in the presence of obvious organic pathology, it will be accepted generally that the more obscure ailments require more exhaustive study and that in these instances the social history may have no inconsiderable clinical significance. Inquiry is directed, therefore, into the patient's personal habits, emotional adjustment, personality factors, busi-

ness life, sex experiences, social contacts, recreational outlets—in short, all those factors in the patient's life which, when developed subtly, intelligently and sympathetically, will enable the physician to arrive at a more profound understanding of the patient and the reasons why he sought medical aid.

PAST HISTORY

With respect to the immediate patient, the personal history is of inestimable value. It is the means whereby the physician can visualize and reconstruct the panorama of a disease process in the patient as it makes its inexorable march down the pathways of Time, modified, aided and opposed by a multitude of factors appearing in the routine daily existence of the patient. The acute forms of disease may be followed in their entirety by a single physician, but the resultant sequelae may not appear for many years and will, therefore, be viewed usually by another physician whose only insight into the why and wherefore of what has transpired is the past history.

It is obvious, therefore, that the amount of information to be ascertained from the past history is considerable, the general trend of the investigation being determined chiefly by the relevant facts pertaining to the present complaints. In general, the outline pursues a consideration of all previous illnesses, the order of their importance being determined, as Meakins has stated, by the sequence of diseases provoking the greatest economic disability to the patient: in childhood, rheumatic fever, tuberculosis which may be manifested by pleurisy or cervical lymphadenopathy, and scarlet fever; in adulthood, heart disease, nephritis, apoplectiform seizures, and finally cancer. Inquiry concerning exposures to possible infectious disease—tuberculosis, for instance—is often illuminating. Of especial importance, moreover, are data concerning various types of traumatic injuries and operative procedures which the patient may have sustained. Such data consider not only the nature of the illness or injury with subsequent surgical treatment, but the name of the surgeon from whom, if necessary, more pertinent information concerning the pathologic process and therapy of the disorder may be gained. The rationale of such investigation is apparent.

Review of Systems. When we come to a consideration of the review of systems, it is fitting that we elaborate considerably on the diverse symptoms appearing within each group of organs, or systems. The writer considers this phase of the history to be outstanding in importance. The review of systems permits an easy organization of many heretofore apparently unrelated symptoms and, perhaps equally important, diminishes the possibility of omission of significant data. This brings us to a consideration of how we think in making a tentative working diagnosis from the history alone. Suppose, for example, that the patient complains of left shoulder pain. Do we, in our minds, dwell upon a parrot-like recital of all causes [illegible] bur- [illegible] bosis, [illegible] up all apparently related facts as determined by data derived from all aspects of the history into the order of the most likely possibilities. For instance, the middle-aged patient who complains of transient left shoulder pain brought on by exertion and relieved by rest is more likely to have angina pectoris than a traumatic bursitis from a football injury. "Grouping" of

symptoms, therefore, is the hallmark for diagnosis. The review of systems in the past history exemplifies this point of view in an admirable manner.

Having established this fundamental concept, let us proceed to an orderly review of the symptomatology of the various systems.

Headaches. Few symptoms are more difficult of interpretation than this relatively common complaint. For a comprehensive discussion of the mechanisms of headache, the differential diagnosis and treatment, the reader is referred to the recent papers by Wolff. Some generalities, however, concerning chronic headache may be permitted in this discussion.

The *headache of eye strain* is usually characterized as a dull, frontal or occipital discomfort appearing in late afternoon or following periods of prolonged employment of the eyes, as reading, sewing, movies and the like.

On the other hand, the *headache of frontal sinusitis* is usually antedated by a history of acute nasopharyngitis, is acute and localized to the frontal area involved, is commonly worse in the morning upon arising due to the secretions accumulated throughout the night, subsides during the day as drainage occurs, recurs in a mild degree toward evening as fatigue develops.

That of *sphenoidal sinusitis* is similar in character but referred frequently to the occipital region; that of *maxillary sinusitis,* to the infraorbital region. All three types are aggravated by forward or lateral movements of the head and imbibition of alcohol.

The *headache due to cervical arthritis* or chronic neck strain is usually distributed to the occipital-cervical area, worse on arising (due to stiffness), subsides somewhat during the day, relieved by massage, heat and other physiotherapeutic measures and rest, and, like most chronic headaches, increases in severity towards evening due to fatigue

Quite similar in distribution, but less localized and more of the nature of discomfort than definite pain, is the *occipital-cervical spasm* characteristic of emotionally unstable and chronically fatigued individuals, particularly women

The *headache of increased intracranial pressure* is usually distributed quite diffusely, mild at first but gradually increasing in severity, though short remissions are not uncommon. It may assume sufficient intensity to awaken the patient during the night and is aggravated by those measures increasing cerebral hyperemia and consequent increase in intracranial tension, as excitement, exertion or straining.

Of especial interest is the *migrainous type* of headache. This form implies the existence of the classical symptomatology. headache, nausea and ocular disturbances To this may be added the therapeutic response to ergotamine tartrate, dihydroergotamine, intravenous nicotinic acid or oxygen inhalations. With respect to the headache, it is usually unilateral, variable in distribution from small to wide areas, difficult to describe but may be intense, pounding, throbbing in character, occurs at irregular and apparently unrelated intervals, and is commonly associated with nausea and vomiting and various ocular phenomena as scotomata, temporary blurring of vision or restriction of the visual fields. The importance of this type of headache lies in the fact that the above symptomatology, especially recurrent nausea and vomiting thought not to be related to the headache, may be mistaken for intra-abdominal pathologic changes which lead to surgical intervention.

Disturbances of the Eyes. The various symptoms related to diseases of the eyes are lacrimation, itching or burning of the conjunctiva, photophobia, redness, pain within the eyeball or the orbit, ocular disturbances, and general symptoms of fever, chills, and malaise. These will be discussed more thoroughly in the chapter on the examination of the eyes. (See Chapter IV.) Suffice it to say that the medical history should consider the possibility of refractive errors and inquiry should be directed, therefore, into the visual acuity, glasses, how long they have been worn, whether the vision is improved, and the like.

Disturbances of the Nasopharynx and Mouth. Principal symptoms of pathologic involvement of the nasopharynx and mouth are coryza, lacrimation, nasal obstruction, salivation, pain and dysphagia. Coryza and the frequently associated and analogous symptom of lacrimation represent an excessive production of mucoid or mucopurulent material from the mucous membrane of the nose and pharynx. The usual etiologic factors are infection, mechanical or reflex nervous irritation, and a hypersensitive response to diverse, but usually nonirritating, agents as pollens, dust, vapors, and the like. That nasal obstruction should be produced is evident in view of the reactive hyperemia and congestion of the mucous membrane, especially that of the turbinates.

A somewhat similar phenomenon is *salivation,* the causes of which may be summarized as follows: (1) psychic disturbances; (2) neurogenic disabilities, e. g., diseases of the medulla oblongata (bulbar paralysis) and chorda tympani (otitis media), disseminated lesions, e. g., encephalitis, and unexplained neuroses; (3) reflex origin from severe visceral pain, especially involvement of the abdominal organs; (4) local inflammation of the salivary glands, tongue or buccal mucosa; and (5) various drug intoxications such as that caused by mercury, iodides, and similar substances.

Onset, periodicity and distribution of pain in the nasopharynx and mouth may lend considerable light as to its origin, as will be developed more fully in the respective chapters concerning the nose, mouth, throat, ear and neck. Suffice it to say that such pain may originate from local involvement, as infections, trauma, tumefactions, dental lesions, and the like; may be referred from similar processes in contiguous or surrounding areas; may take origin from various systemic diseases, as acute rheumatic fever, diphtheria, agranulocytic angina, and mumps; and, finally, may be neurogenic in origin, as the various neuralgias. Whether or not dysphagia or painful swallowing is associated will depend upon the development of acute or chronic lesions of the fauces and esophagus.

Disturbances of the Ears. Symptoms referable to various diseases of the ears are pain, discharge from the ears, disturbances in hearing, and disturbances in equilibrium, as vertigo, dizziness, and the like. This is covered more fully in the chapter concerning examination of the ears. (See Chapter VI.)

Disturbances of the Neck. The three outstanding symptoms of diseases of the neck are disturbances in movement, pain and swelling. The causes may be classified into the common etiologic factors of disease: congenital anomalies, trauma, infections, tumors, degenerative and functional entities. The history combined with physical examination of the neck affords no inconsiderable amount of information, not only of local disorders but likewise of a wide variety of systemic disturbances. Bearing in mind

that the neck is readily accessible to examination it is a sad commentary that we tend to neglect examination of this portion of the anatomy.

Disturbances of the Respiratory System. Here we must consider broadly those symptoms arising from involvement of the respiratory tree anywhere from the larynx to the pleura. Symptoms may be present, either continuously or intermittently, yet the physical examination reveals no underlying basis for their existence. As in disease elsewhere, the sequence of events in certain pulmonary diseases lends strong evidence to the diagnosis of that form of pulmonary involvement.

Disturbances of Phonation. The most common symptom in diseases of the larynx is that of disturbances of phonation. Although this disturbance of speech may vary from a mild hoarseness to complete loss of the voice, it must be appreciated that the degree of speech impairment is not proportional to the severity of the underlying lesion. Generally speaking, alterations in phonation are due to four factors: (1) local lesions, either of inflammatory or neoplastic nature; (2) paralyses of vocal cords, either central or peripheral in origin; (3) hysteria; and (4) spasmodic affections of the vocal cords, as in tetanus, tetany, and the like. Early diagnosis of the cause of dysphonia is extremely important inasmuch as therapy of these conditions in the early stages offers the greatest hope of recovery.

Stridor. Stridor represents auditory evidence of obstruction anywhere in a major portion of the respiratory tree, as in the epiglottis, larynx, trachea, and partial occlusion of both main bronchi. It is usually present during the inspiratory phase, though it may be expiratory in nature or persist throughout the whole respiratory cycle. Without listing the various causes of stridor, it is apparent that stridor may be produced by any lesion within the major respiratory tree, whether it be inflammatory, neurogenic, allergic, congenital, neoplastic, spasmodic or traumatic in origin, as well as compression of the air passage by similar lesions in the surrounding structures. Whether or not obstruction of one main bronchus will give rise to stridor is doubtful.

Wheezing The writer has been increasingly impressed with the significance of wheezing in pulmonary disease. It is described variously. Some patients discern a peculiar clicking sound in their chest during inspiration or expiration, many experience a tight, smothering sensation indefinitely localized in the chest, others manifest the full blown picture of wheezing as characterized by difficult inspiration and prolonged expiration. It may be aggravated by laughing, temperature changes, drafts of cold air, air conditioning, exercise, alcoholic imbibition and recurrent upper respiratory tract infections. Cough as well as dyspnea is usually associated The wheeze may be so loud as to be audible to the patient's family, friends or the examiner. Frequently, patients wheeze during sleep in which circumstances the information must be supplied by the patient's wife or members of the family; occasionally, nocturnal asthmatic paroxysms may occur. The pathologic physiology of wheezing appears to be that of partial bronchial obstruction and usually denotes, therefore, exudate or other obstruction in the respiratory tract anywhere from the larynx to the peripheral alveoli

Cough. Cough may be considered as a reflex symptom produced most commonly by alterations in the quantity and viscosity of the secretions of the mucous membrane of the trachea, bronchi, and, occasionally, the larynx. Similarly, the changes in the nature of the secretions in the respiratory

tree determine the character of the cough, i. e., whether it is dry, hacking, paroxysmal, explosive, persistent, and, of equal importance, whether it is productive or nonproductive. The productive type indicates an abundance of secretion and the nonproductive type suggests a relatively dry lining of the respiratory tract. The cough reflex is, withal, one of the most important protective mechanisms of the lungs. At times, the character of the cough may be sufficiently distinctive to suggest certain anatomic or functional disturbances, as the "brassy" cough produced by mediastinal tumors impinging upon the trachea.

Expectoration. This is commonly the most neglected symptom of diseases of the chest, yet observations of the sputum only too frequently make the etiologic diagnosis. For example, consider a consolidated area of the lungs. Neither the physical examination nor the roentgenologic studies will determine the etiology; that alone can be determined from studies of the sputum, grossly and microscopically, combined with the clinical picture. Data concerning the sputum include: twenty-four-hour volume, color, consistency, odor, presence of foreign particles, cellular products and bacteria. From the point of view of history taking, microscopic studies obviously do not apply.

VOLUME OF SPUTUM. The chief pulmonary diseases producing large volumes (over 100 cc. daily) of sputum are pulmonary edema, lung abscess, bronchiectasis, bronchial asthma, and advanced pulmonary tuberculosis (Osgood). Should a fistulous connection exist between a bronchus and an extrapulmonary collection of pus, as empyema, subphrenic abscess or liver abscess, the volume of sputum expectorated will likewise be considerable. The twenty-four-hour volume also has prognostic significance: increasing amounts of sputum in abscesses, cavitation, or bronchiectasis suggest extension of the suppurative process; decreasing quantities indicate healing; sudden cessation of expectoration suggests plugging of a bronchus which may demand reestablishment of drainage if an increase in constitutional symptoms is to be prevented.

CHARACTER OF SPUTUM Whether the character of the sputum be mucoid, mucopurulent, purulent, hemorrhagic or serous will be determined by the nature of the inflammation causing it. Due to its albuminous content, the sputum of pneumococcic pneumonia is characteristically so tenacious that the container may often be inverted without spillage. The sputum of the three chief suppurative lesions of the lungs, bronchiectasis, lung abscess and gangrene, tends to separate into three layers [illegible]

[illegible]

of hemoptysis are bronchiectasis, pulmonary tuberculosis, mitral stenosis, pneumonias of all types, pulmonary infarction, and malignant neoplasms. Practically speaking, the clinician usually considers hemoptysis as being tuberculous in origin until proven otherwise. There are certain color variations of some significance: greenish color may indicate jaundice or Ps aeruginosa infection; black sputum suggests anthracosis; and a characteristic "anchovy sauce" appearance of the sputum points to rupture of an amebic abscess of the liver into a bronchus.

ODOR OF SPUTUM. Upon the sensibilities of the patient and physician rests

the question of odor of the sputum. Admittedly, a foul, putrid odor is present in putrefactive lesions of the lungs, as lung abscess, lung gangrene, certain forms of bronchitis, bronchiectasis and necrotic neoplasms, but, as Osgood has stated, odor is more often absent than present.

Dyspnea. Meakins defines dyspnea as the "consciousness (of the patient) for increased pulmonary ventilation." Bearing in mind that respiration is a more or less involuntary, unconscious act controlled by the respiratory center in the medulla, which, in turn, is activated by the pH of the blood, it is obvious that many pathologic and functional derangements may produce dyspnea.

CAUSES OF DYSPNEA. Meakins classifies the causes of dyspnea into six broad groups: (1) acidosis secondary to metabolic disturbances, as exercise, diabetes, nephritis, hyperthyroidism and hyperinsulinism; (2) oxygen deprivation resulting from circulatory deficiencies, anemia and high altitudes; (3) organic neurologic lesions near the respiratory center; (4) diverse pulmonary diseases in which there is either obstruction to the respiratory ventilation, diminished alveolar air space, or decreased pulmonary vascular circulation; (5) interference with the respiratory effort resulting from altered intercostal or diaphragmatic action; and (6) neuroses. For the consideration of dyspnea as a symptom of diseases of the respiratory tract, suffice it to say that any factor interfering with the exchange of carbon dioxide in the lungs and the acquisition by the blood of oxygen as it passes through the pulmonary circulation will give rise to dyspnea

Cyanosis. Normally, the hemoglobin of the arterial blood as it approaches the peripheral capillaries is 95 per cent saturated with oxygen. Should deficient oxygenation of the hemoglobin occur and the percentage of reduced *hemoglobin in the capillary blood exceed 10 per cent, a bluish tinge* to the mucous membrane and skin, termed cyanosis, results. The intensity of the cyanosis is proportional to the degree of reduced hemoglobin. Although there are many causes of cyanosis, the chief respiratory causes, like those of dyspnea, are any factors bringing about inadequate respiratory exchange, as obstruction of the larynx or trachea, diffuse bronchial obstruction as in asthma, altered permeability of the alveolar epithelium ascribable to inflammatory, chemical or circulatory disabilities, and paralysis of the respiratory muscles

Pain. Extensive disease of the respiratory system may be present without *the production of pain. Though a dry, irritating sensation in the region of* the larynx and behind the suprasternal notch and sternum may accompany certain affections of the larynx, trachea and bronchi, the presence of pain usually indicates disease of the pleura Here, again, it must be recalled that the visceral pleura is devoid of nerve endings but the parietal pleura is extremely sensitive. Pleuritic pain possesses several characteristics. It is usually localized over the site of pleural involvement, is severe and arresting in character, and is usually aggravated by deep inspiration or coughing Inasmuch as the greater respiratory excursion takes place in the lower lobes of the lungs, as contrasted to the apical areas, pleuritic pain appears com*monly in the lung bases. Often it is described* as being knifelike, stabbing or cutting in character.

Disturbances of the Cardiac System. As Paul White has emphasized, the first heart symptom is the keystone on which further examination of the cardiac patient depends. Inasmuch as the chief symptoms of heart disease—dyspnea, substernal or precordial pain, and palpitation—may

not only be simulated by extracardiac phenomena but may readily be confused with each other, one cannot stress too greatly the development of the symptoms of the cardiac patient, with careful observations concerning time, character, intensity, variability, and relationship to extraneous or precipitating factors. In addition to the significant symptoms of heart disease mentioned above, many symptoms of a varied nature consequent to disturbances in function of other organs, particularly the lungs, gastrointestinal tract, and brain, may develop.

Alterations of Respiration. This considers three fundamental alterations of respiration ascribable to heart disease: dyspnea, cardiac asthma, and Cheyne-Stokes breathing as exemplified in the next chapter.

Although *dyspnea* may arise from many other causes, as acute and chronic pulmonary diseases, mediastinal diseases, diaphragmatic hernias, and certain nervous conditions, shortness of breath on exertion remains one of the earliest and most significant symptoms of heart disease. At first the cardiac patient notes mild intolerance to exertion that ordinarily has provoked no discomfort. This progresses as the cardiac function decreases, often accompanied by dependent edema and other evidences of congestive failure, until the dyspnea becomes so profound as to render the patient uncomfortable at rest and in the upright position—*orthopnea.* At this time, further evidences of advanced congestive heart failure may be found on examination—hepatomegaly, dependent ankle, scrotal and sacral edema, ascites or hydrothorax, and marked pulmonary congestion as noted by bilateral basal rales in the lungs. Though the mechanism of this dyspnea is not definitely established, the preponderant evidence suggests that it is due either to diminished vital capacity as a result of pulmonary congestion secondary to failure of the left ventricle or as the result of a reflex action on the respiratory center initiated by engorgement of the pulmonary circulation (White).

When pulmonary congestion occurs suddenly, either as the result of failure of the left ventricle or of tachycardia in instances of marked mitral stenosis, profound dyspnea characterized by asthmatic breathing develops. This is paroxysmal dyspnea or *cardiac asthma*, and, as Hope pointed out in 1832, is bronchial asthma occurring in a patient with heart disease. Generally speaking, the attacks are precipitated most commonly at night (paroxysmal nocturnal dyspnea) when the patient lies asleep in the recumbent position, though not infrequently attacks may occur in the daytime following any unusual exertion. The attack may be accompanied by a hacking cough and a sense of substernal oppression In the milder forms, relief is obtained by assuming the upright position; in the more severe forms, the condition is serious Paroxysmal dyspnea occurs most frequently in those types of heart disease leading to severe strain on the left ventricle, as hypertension, aortic insufficiency and stenosis, coronary thrombosis, and, rarely, advanced mitral stenosis in which sudden acceleration of the heart rate either by tachycardia of exertion or of paroxysmal character floods the pulmonary circulation.

Cheyne-Stokes breathing is a form of respiration characterized by periods of apnea alternating more or less regularly with periods of hyperpnea. Though it may occur in many other conditions such as uremia, affections of the central nervous system, hypnosis induced by chloral hydrate and morphine, high altitudes and, to a mild degree, in infants and elderly

patients, it is a common observation in advanced congestive failure ascribable to arteriosclerotic and hypertensive forms of heart disease. In general, this bears a grave prognosis During the period of apnea the patient may become drowsy and fall asleep to be awakened suddenly by intense respiratory effort (hyperpnea) which lapses, after a few seconds to half a minute or so, to another period of apnea. Levine has emphasized that the significance of this form of breathing in advanced congestive failure is that the period of hyperpnea not only interferes with rest of the cardiac patient but the increased muscular activity of the thoracic cage augments venous return to the right ventricle, thus aiding in the perpetuation of the pulmonary engorgement. A vicious cycle is thereby created which warrants our attention from a therapeutic point of view.

The most tenable explanation for Cheyne-Stokes breathing is that offered by alterations in the pH of the blood as a result of carbon dioxide exchange in the lungs. During apnea, the carbon dioxide increases in the blood, the pH is lowered, until, finally, the respiratory center is stimulated to intense activity, during hyperpnea, the carbon dioxide diffuses through the lungs into the expired air, the pH of the blood is accordingly raised, the stimulus on the respiratory center decreases until it is eventually lulled into inactivity, and another period of apnea ensues.

Pain. Evaluation of the type of precordial or substernal pain believed to be due to heart disease is of paramount importance. In many instances, pain alone forms the basis for diagnosis, as in angina pectoris and, frequently, coronary thrombosis. White describes seven types of pain in the chest for which the heart and great vessels may be held responsible: (1) precordial aching or heartache; (2) substernal oppression ascribable to coronary artery insufficiency; (3) angina hypercyanotica; (4) pain of acute pericarditis; (5) pain of acute rheumatic carditis; (6) pressure pain from aortic aneurysms; and (7) the rending pain of dissecting aneurysms of the aorta.

The commonest type of "heart pain" is *precordial aching* or distress. The characteristics of this type of pain are variable. It may be mild, moderate or severe, transient, fleeting, or more or less permanent. Though it may radiate to various points in the chest or even to the arms, thus permitting confusion with anginal pain, the pain is generally limited to the precordium. An important point in its differentiation is the presence of precordial tenderness in the more severe forms. Generally speaking, this type of heart pain may be attributed to oversensitiveness of the nervous system from fatigue, premature beats or extrasystoles, or an enlarged, forceful heart thumping against the chest wall. It rarely indicates heart disease per se; in fact, it most commonly suggests the nonexistence of heart disease and is, therefore, reassuring to the examiner. Precordial aching occurs most commonly in hypersensitive individuals and in instances of neurocirculatory asthenia.

Substernal oppression, on the other hand, bears a much more grave significance; it generally indicates coronary artery insufficiency whether it be due to spasm, anemia, thrombosis, or embolism. As with precordial pain, the characteristics of substernal pain vary from mild to severe forms, transient to permanent pain necessitating opiates for relief, and may be localized or radiate over chest, to neck, down arms, or even to the epigastrium, thus simulating an acute surgical abdomen. In the early forms, substernal oppression appears upon exertion or excitement and is relieved

by immediate rest. Quite frequently, this occurs in early morning as the patient hurries to work whereas the precordial pain of neurocirculatory asthenia develops later in the day as fatigue appears.

When the pain of substernal oppression assumes certain characteristics, such as being precipitated by those factors increasing the demands on the heart, lasting but a few minutes and disappearing on rest or following the therapeutic use of vasodilator drugs as the nitrites, it is called *angina pectoris*. When the pain tends to last for several hours to several days, may have had its onset during sleep or at rest, is accompanied by evidences of circulatory insufficiency as shock, lowered blood pressure or vasomotor collapse, is not relieved by vasodilator drugs or rest but demands heavy sedation, and is accompanied by general constitutional findings of fever, leukocytosis and increased sedimentation rate, the diagnosis of *coronary occlusion* is usually established.

A few patients with advanced mitral stenosis or other forms of heart disease producing severe cyanosis occasionally note heavy precordial or substernal pain, with or without radiation. This is called *angina hypercyanotica;* it may be due to myocardial anoxia (White).

Most patients with acute and chronic pericarditis note no pain, though an acute pericardial effusion may produce a dull, precordial oppression. If certain portions of the parietal pericardium, particularly that adjoining the pleura and outer diaphragmatic portions, are involved, a disagreeable sticking or stabbing pain similar to pleurisy may result. As with pleuritic pain, this pain is usually accentuated by respirations and, if the diaphragmatic portion is involved, may be referred to the left shoulder.

During the first few days of a severe rheumatic infection in childhood, precordial pain of more intense character than that of neurocirculatory asthenia may be present. Its meaning is not clear.

Erosion of contiguous structures anywhere in the chest, as bones, cartilage and nerves, by an aortic aneurysm results in excruciating, persistent pain of such severity as to demand therapeutic relief either by opiates or alcohol injection of nerves. In those instances where examination of the patient permits the diagnosis of aneurysm with subsequent erosion, the explanation is clear.

Should a dissecting aneurysm develop, in which there is extensive separation of the media of the aortic wall perhaps throughout its entire length from aortic valves to the common iliac arteries, intense, excruciating, *substernal pain* follows immediately, may radiate, as with coronary artery pain, to any point in the chest and often to the abdomen and down the legs, and tends to last for hours or until death secondary to rupture of the aorta anywhere in its course intervenes. The pain of dissecting aneurysm reaches the acme of its intensity immediately whereas that of coronary insufficiency requires a few minutes to reach its greatest intensity.

Palpitation. Palpitation, or throbbing, bears little significance as an indication of cardiac disability. It most frequently occurs as the result of relatively unimportant disturbances of cardiac rhythm, as premature beats, paroxysmal tachycardia and tachycardia consequent to excitement, exertion, thyrotoxicosis, severe anemias, climacteric, certain infections as tuberculosis, and toxic effects from alcohol, coffee, tobacco and fatigue. Occasionally, palpitation is noted with important disturbances of cardiac rhythm, as auricular fibrillation, auricular flutter, and heart block.

Extracardiac Symptoms. As noted above, a wide variety of symptoms not directly related to the heart disease may develop as a result of secondary disturbances in various organs, particularly the lungs, gastro-intestinal tract, and brain. These symptoms are important in that they may not only aid in the establishment of the diagnosis of cardiac impairment but may likewise arouse such discomfort as to prompt the patient to seek medical aid in the first place. The large number of such symptoms incidental to heart disease include cough, hoarseness, hemoptysis, faintness, syncope, dizziness, headaches, fatigability, nervousness, insomnia, various sorts of abdominal pain or discomfort, anorexia, gaseous eructations, and pain in the legs due to inadequate blood supply to the muscles (intermittent claudication)

Disturbances of the Gastro-intestinal System. When we recall that the gastro-intestinal system is relatively inaccessible to physical examination, it becomes readily apparent that elicitation of the diverse symptomatology of this system is extremely important. The gastro-intestinal system is unique in two respects: not only may organic lesions of this system develop to an advanced degree before physical findings become apparent to the examiner, but reflex derangements of the alimentary tract secondary to functional disturbances elsewhere in the body are common No inconsiderable knowledge of the physiology of the gastro-intestinal tract is necessary, therefore, for intelligent interpretation of abnormalities of this system.

Although examination of this system will be stressed in greater detail in the chapter concerning the abdomen (Chapter XII), for the purposes of history taking it behooves us to discuss this system from a broad point of view Moreover, it will make for clarity if we subdivide the system not into symptoms per se but into organs, bearing in mind that the symptoms of gastro-intestinal disabilities may be produced by functional or anatomic derangements in more than one organ. The key to the history of this system, therefore, is two-fold: grouping of symptoms and the sequence of events Furthermore, it must be appreciated that an accurate and detailed history, valuable though it may be, does not permit an accurate diagnosis; further studies are necessary: physical examination; analysis of the gastric contents and the stool; roentgenologic studies; various endoscopies notably esophagoscopy, gastroscopy and proctoscopy; and laboratory studies of blood, urine, stool and the like.

Esophagus. The symptoms of esophageal difficulties are four-fold: difficulty in swallowing, strangling or choking, pain and regurgitation.

Difficulty in swallowing, *dysphagia,* may be manifest at first only to solid foods, the patient noting that an additional effort or frequent sips of liquid will aid the process of deglutition. This can be explained not only on a mechanical basis but by the observation that the peristaltic force of the esophagus increases if the swallowing process is repeated a few times. Further progress of the underlying condition may later render swallowing liquid food difficult. *Choking,* or strangling, is a reflex mechanism consequent to sidetracking of food into the larynx or undersurface of the epiglottis; if the condition is persistent, paralysis of the pharyngeal musculature may be suspected.

Of less importance in diseases of the esophagus is *pain,* which, if present, is usually substernal in location. Generally speaking, it may be considered

due to spasm resulting from various irritative lesions in the esophagus or to pressure of esophageal lesions upon surrounding structures. The symptom of *regurgitation* is an interesting and, withal, prominent feature of esophageal abnormalities Often, more than a liter of retained food may be regurgitated. It does not always signify an acquired obstructive lesion, for such lesions as a congenital diverticulum or atonic dilatation of the esophagus may give rise to regurgitation. Clinically, the majority of esophageal disabilities are due, in the order of frequency, to cancer, spasm and stenosis.

Stomach. As emphasized by Bloomfield, the most important consideration in the history of stomach disorders is to decide whether they are organic or functional in origin. The organic diseases of the stomach may be suggested by vomiting of blood, passage of blood in the stool, recurrent vomiting of ingested food (pyloric obstruction) and intense, localized epigastric pain and tenderness ascribable to localized or generalized peritonitis.

Excluding those symptoms, Bloomfield classifies all other stomach complaints into a large, variable group under the heading of "indigestion." These symptoms—anorexia, nausea, vomiting, belching, fulness, epigastric distress or burning, and sour eructations—are familiar to everyone, physician and layman alike. One of the most prominent features of the digestive complaints is the vague, indefinite, disagreeable sensation in the epigastrium which is described in variable terminology by individual patients and which may be localized to the epigastrium or spread more or less diffusely over the abdomen and even to the chest. Should the distress be accompanied by a choking or "lumpy" sensation in the throat and regurgitation of sour fluid, it is called "heartburn," or pyrosis The next most important symptom of indigestion, according to Bloomfield, is that of belching of air which has been swallowed either deliberately or unconsciously. Anorexia and nausea are frequently present, though vomiting occurs rarely unless induced by the efforts of the patient.

Considerable variation in the description of these symptoms will be manifest from patient to patient, dependent on the patient's powers of expression and degree of sensitivity to visceral phenomena. In addition, various symptoms referable to the bowel may accompany the picture, as constipation, abdominal cramps, passage of mucus in the stool (mucous colitis), and possibly intestinal distention.

Having recognized a large group of symptoms comprising the general heading of "indigestion," what causes the indigestion? That the indigestion is due to actual sensitiveness of the stomach has been proven untenable in view of the fact that the stomach mucosa is relatively insensitive to various chemical and physical stimuli. On the other hand, introduction of a balloon into the first portion of the duodenum and subsequent inflation produces symptomatology similar to that of indigestion. Deflation of the balloon results in immediate disappearance of the pain (Polland and Bloomfield) These studies suggest, therefore, that indigestion is a reflex phenomenon mediated via the autonomic nervous system and that abnormal tension or spasm of the gastro-intestinal tube serves as the underlying stimulus When we recall, moreover, the complex musculature of the stomach and the mechanism of the sphincteric control, the presence of indigestion in the various derangements of the stomach, slight though they may be, becomes intelligible.

The intimate relation between the symptoms of indigestion and the

autonomic nervous system leads Bloomfield to divide the causes of indigestion into three groups: (1) Any lesion in the stomach leading to abnormal tension or spasm, particularly of the pylorus or cardia, will provoke the symptoms of indigestion. This implies that both carcinoma and peptic ulcer may give rise to the same symptoms, the differential diagnosis being based on evidences other than the symptoms of indigestion. (2) In view of the fact that the majority of the abdominal viscera have a common source of autonomic innervation, spasm or tension of the stomach, especially of the pylorus, may readily arise from organic abdominal disease outside the stomach, as appendiceal or biliary tract involvement. Too, symptoms of indigestion are frequent manifestations of congestive failure or coronary occlusion. (3) A wide variety of purely nervous or mental influences may likewise produce the symptoms of indigestion. In fact, Bloomfield concludes that this form of indigestion is probably the most common type, the patient usually being of a high-strung temperament and the precipitating factors being directly related to stress, worry, and tension or to faulty habits of eating, especially rapid eating.

From this discussion, it will be recognized that the diagnosis of disorders of the stomach from the history is fraught with difficulty. Suffice it to say that the physician should make inquiry into the onset and duration of symptoms, their intensity, their relationship to meals, what factors relieve them, and their relationship to any possible precipitating factors outside the stomach. The diagnosis itself will rest on the history and further data derived from the physical examination, roentgenologic studies, gastric analysis and stool examination.

Intestine. As symptoms referable to disorders of the stomach may be on an organic or functional basis, so may intestinal symptoms be due to similar etiologic factors. Intestinal symptoms are quite limited in their forms of expression—constipation, diarrhea, pain or obstructive symptoms. Again, as with the stomach, the final diagnosis is not permitted by the history alone but must follow from additional studies of the stools, proctoscopy, roentgenologic investigation and exploratory laparotomy.

CONSTIPATION. When we come to the discussion of constipation, considerable difficulty arises in determining the difference between normal bowel habits and the pathologic types, for evacuation of the bowels is not a wholly unconscious habit, especially in the elderly, and constipation is probably the most frequent human complaint (Bloomfield). Generally speaking, constipation results from any factors delaying the forward movement of the intestinal contents, whether this be in the nature of anatomic obstruction anywhere from the esophagus to the rectum or of sluggish peristaltic activity secondary to a combination of factors—irregular habits of defecation, faulty dietary intake particularly of bulky foods, lack of exercise, obesity, and diverse nervous and mental influences Clinically, the latter type, i. e., sluggish peristaltic activity, is far more common. Bloomfield concludes that the division of constipation into "spastic" and "atonic" types is of little diagnostic value. Whether or not constipation may give rise to other remote symptoms, as fulness and pressure in the lower abdomen, anorexia, headache, and mental and physical apathy, is a moot question.

DIARRHEA The contrast of constipation is an abnormal looseness of the bowel movements termed diarrhea. Whereas constipation is most commonly due to functional derangements of the bowel habit, diarrhea may be attri-

buted most commonly to local pathologic causes within the intestine. As with constipation, however, a wide variety of factors may produce diarrhea, a list so large as to be beyond the scope of this discussion. The more serious grades of diarrhea frequently result in associated symptoms of cramplike abdominal pain of varying severity, perianal burning or discomfort, various degrees of weakness and prostration which are dependent upon the loss of fluids and ingested foods, and the toxic effects of the underlying disease process.

The pain derived from abnormalities of the small intestine is described usually as occurring about the umbilicus or in the middle zone of the abdomen; that of the large intestine, in the lower third of the abdomen without any definite localization. Both may vary from the sensation of fulness to that of acute abdominal colic suggestive of obstructive phenomena. In this connection it must be recalled that the mucosa of the intestine, like that of the stomach, is insensitive to tactile stimulation, consequently the mechanism of intestinal pain lies within any factors producing spasm or tension of the intestinal tube with resultant stimulation of the autonomic nervous system and pylorospasm usually as the end result.

STOOLS. From what has been said, it is evident that inquiry into the character of the stools, with special studies later (mucus, pus, blood, search for cysts, ova or parasites, and chemical and bacteriologic investigation), reveals no inconsiderable amount of information concerning the nature of the abdominal complaint. The examiner is interested in the form, consistency, color, volume, and number of stools. The clay colored stool of biliary tract obstruction, the black stool of massive hemorrhage in the gastrointestinal system, the large, putrid stool of steatorrhea and sprue, the watery, greenish stool of intestinal diarrhea, the dry, hard (scybalous) stool of constipation, all afford definite clinical information

Liver. The liver may be riddled with advanced pathologic entities yet provide no symptoms whatsoever. Consequently the history is of little value in the diagnosis of liver disorders. Generally speaking, two important signs, which may likewise be symptoms to the discerning patient, may be noted: the presence of liver enlargement or a lump in the right upper quadrant, and jaundice. Occasionally, pain in the epigastrium or right upper quadrant is present. In addition, various symptoms of indigestion and general lethargy may be present, either persistently or recurrently, for some time for [illegible]

Biliary [illegible]
in fact, i [illegible]
right upper quadrant pain and tenderness, possible fulness or lump, and, if the condition be acute, the symptoms of an acute infection such as fever, chills, prostration. Bloomfield is convinced that the symptoms of so-called "gallbladder indigestion" differ in no way from those of indigestion due to any other cause. Therefore, these symptoms offer no aid in the diagnosis of chronic diseases of the biliary system.

Pancreas Disturbances of the pancreas must be inferred from indirect evidences of alterations in secretions or remote effects, such as jaundice consequent to biliary obstruction due to carcinoma of the head of the pancreas. Bearing in mind that the pancreas has a dual function of secretion, deficiencies in the internal secretion result in diabetes mellitus, whereas derangements of the external secretion (absence of ferments) alter the

digestion of proteins and fats in the intestinal tract, the stool containing abnormally large quantities of fat and muscle fibers.

Peritoneum Generally speaking, the symptomatology of affections of the peritoneum varies with the underlying condition, but that of acute peritonitis is usually clearcut—sudden onset of severe abdominal pain, localized or generalized, followed by the evidences of acute intoxication, as nausea, vomiting, fever, prostration and collapse.

Disturbances of the Genito-urinary System. Surprisingly enough, Meakins found, in an analysis of the histories of 1,000 cases, that symptoms referable to the genito-urinary tract, though actually second in frequency to those of the gastro-intestinal tract, were complained of infrequently unless the examiner made special efforts to ascertain their existence. Meakins concludes that this hesitancy on the part of patients to present their genito-urinary symptoms reflects that these symptoms are more or less intermittent and rarely disabling, and that patients from a sense of privacy are reluctant to discuss them. Nevertheless, the symptomatology of the genito-urinary system reveals very pertinent information

Frequency of Urination This is the most common symptom of genitourinary disorders. In instances wherein habit spasm may be excluded, frequency is symptomatic of irritative lesions in the renal pelvis and bladder, distention, and increased volume of urine (polyuria). Polyuria, in turn, suggests a relatively large group of medical disorders—diabetes mellitus, diabetes insipidus, Bright's disease (glomerulonephritis), ingestion of excessive fluid, and emotional and neurologic disorders. Corroborative evidence of these medical disorders is furnished by the presence of nocturnal frequency accompanied by nocturnal polyuria. On the other hand, frequent urination of small amounts generally indicates local pathologic alterations in the lower urinary tract of concern to the surgeon, the discussion of which will be presented in more detail in the urologic chapter. (See Chapter XIV.)

Similarly, oliguria may arise by a two-fold mechanism: reduction of glomerular filtration as a result of the local and general factors listed above, and mechanical impediment.

Hematuria The presence of bleeding at any point along the urinary tract will give rise to hematuria. The "smoky" urine of glomerulonephritis describes the intimate mixing of red cells with the urine consequent to glomerular damage. Bleeding at the onset of urination originates in the urethra; bleeding at the end of urination suggests pathologic evidences in the bladder outlet or prostatic urethra; bleeding throughout all of urination arises from the kidneys, ureters, bladder and prostatic urethra.

Pain This assumes several characteristics. Unilateral pain in the back or abdomen points to kidney or ureteral involvement. If the unilateral pain be extremely sharp and tends to radiate to the bladder or testicles, ureteral obstruction, most commonly due to a stone, is suggested (ureteral colic). Dull pain across the lower back may be due to chronic diseases of the prostate gland and seminal vesicles; suprapubic pain, to involvement of the bladder or intestine; pain in the groins, testicles or perineum, to lesions of the genitalia. Burning or pain throughout urination may be ascribed to lesions of the urethra; pain at the end of urination, to vesical neck conditions.

Pyuria. The presence of gross pus in the urine may be attributed to inflammation anywhere in the urinary tract.

Difficult Flow of Urine. Difficulty in starting the stream of urine may be purely nervous in origin or due to overdistended bladder or obstruction, usually prostatic in nature. Dribbling or a small stream suggests urethral stricture, prostatic obstruction or neurologic affections.

Examination of Urine. Observations by the discerning patient include the presence of various pigments in the urine, as biliary pigments, blood, pus, passage of shreds (lower urinary tract involvement) and changes in color indicative of alterations in specific gravity, as the serous, colorless urine of diabetes insipidus. That these observations should be confirmed by urinalysis and other indicated studies is obvious. One is not justified in considering albumin, casts, occult blood and pus as symptoms; they are signs of genito-urinary tract involvement.

Constitutional Symptoms. Chills and fever suggest an inflammatory lesion in the urinary tract. Dependent or generalized edema, headaches, nausea and vomiting, dyspnea, pallor, weakness, prostration, twitchings and convulsions, visual changes—all are common symptoms of extensive renal disease; the reader is referred to standard texts of medicine for a discussion of their physiology. The recent monograph by Addis concerning glomerular nephritis is especially recommended.

Disturbances of the Nervous System. The nervous system is intimately related to the body as a whole and a general evaluation of the patient is nowhere more important than relative to diseases of the nervous system (Spurling). It is also true that a carefully developed neurologic history can contribute more to neurologic diagnosis than in any other branch of medicine, particularly in the differentiation of the functional and organic types of nervous diseases The intelligent patient is a surprisingly keen observer and the examiner should afford the patient an opportunity to relate what he knows about his neurologic disorder. The existence of various medical conditions of the heart, lungs and the gastro-intestinal tract, and of anemias, malnutrition, and systemic infections, must not be overlooked. Inquiry should be directed to a family history of nervous disorders, such as epilepsy, brain tumors, behavior disturbances and hereditary predispositions. In the patient's past life, pertinent information should be obtained concerning his development, age at which the patient began to walk and talk, progress in school, convulsions during childhood, infectious diseases which may involve the nervous system (scarlet fever, encephalitis, meningitis, otitis media, syphilis, etc.), injuries (at birth and subsequently), standard of living, social habits with especial reference to his recreations and vices, and marital and sexual status.

Symptomatology. With regard to the symptomatology directly related to disorders of the nervous system, the examiner should obtain, if possible, a clear picture of the chronologic sequence of events, often recording the symptoms in the patient's own terms At times, direct questioning will be necessary to clarify points in the patient's story. Was the onset sudden or gradual? Was the course progressive or have there been remissions and exacerbations? As the history unfolds, further questions will usually suggest themselves to the physician. For example, the symptom of pain should be exhausted as to its appearance, location, radiation, periodicity, and methods of obtaining relief. For the sake of organization, however, the physician will do well to pursue the line of questioning along a definite, anatomic order: head, trunk, sphincters and extremities. Relative to the *head,* inquiry

There is not even agreement about the source of the presumed nerve fibres around capillaries. Stohr[109] said they come from nerve fascicles in the pericapillary tissues, whereas Nelemans[110] maintained they are continuations

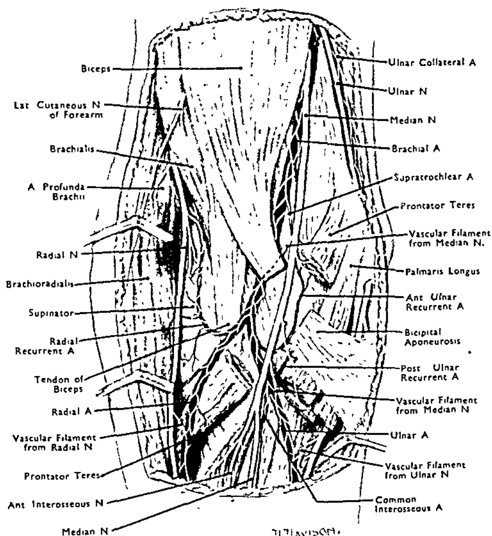


FIG 10
Paravascular nerve filaments accompanying brachial, radial and ulnar arteries

from the periarteriolar nerve plexuses, a view with which one is in personal agreement.

In arteriovenous anastomoses the thick walled arteriolar segment is surrounded by a cuff of unmyelinated fibres which ends rather abruptly at the level of the venous segment (Masson[111]). Some offsets from these glomeral

thinly myelinated or unmyelinated axons and is a mixture of afferent and efferent *fibres*. The deeper fibres in the media are generally of the finer unmyelinated or thinly myelinated types, but some thicker *fibres do reach the* zone deep to the intima. Nerve cells or small ganglia are often found in close association with the adventitia of certain vessels such as the visceral (Fig. 12), vertebral, carotid (Fig 13) and cerebral (Fig. 14) arteries, and Lazorthes[24]

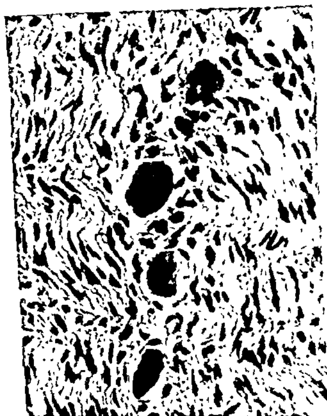


FIG. 13
Small group of nerve cells lying between fibres of internal carotid nerve (Human H and E ×380)

claims he has found them also alongside the facial and radial arteries; most are efferent sympathetic or parsympathetic neurons which have migrated along the vascular nerves, but those alongside the internal carotid arteries may represent the cephalic extremities of the sympathetic trunks (Mitchell[115, 116]).

There is much argument about the exact ultimate *ramifications of* autonomic efferent fibres in the heart, blood vessels and other structures Several observers have described bulbous, loop or free endings in, on, or between the muscle fibres (Dogiel,[112] Lapinsky;[117] and Woollard[63]), while others believe that the terminal nerve fibres or fibrillae, which are often beaded or

vascular plexus from which small groups of fibres penetrate into the vessel walls, often alongside the vasa vasorum, to ramify and form much finer networks in the adventitia and in the subjacent media (Fig. 11). Some fibres reach the junctional area between the media and intima, but it is doubtful if they enter the latter. These appearances led Dogiel,[112] Cajal [113] and Gläser[114]



FIG. 12
Small ganglion in adventitia near origin of right renal artery from abdominal aorta (Human · H and E. × 130)

to describe superimposed and interconnected networks; the first and best defined in the adventitia; a second, very delicate, in the media; and a third, often difficult to distinguish, in the zone between the media and intima The existence of the deeper networks partially nullifies any attempt to produce denervation off arteries, and perhaps of viscera and other structures they supply, by stripping of their adventitial coats, a procedure now largely discarded clinically but not experimentally: the procedure is rendered still more futile by the fact that as the vessels pass peripherally their perivascular plexuses receive reinforcing filaments at intervals from nearby mixed nerves (p 19). The adventitial network contains some myelinated and numerous

varicose, end by joining syncytially in a delicate terminal reticulum or ground plexus (Figs. 15, 16), the finer meshes of which may closely embrace individual muscle cells (Fig. 17), and which has small interstitial cells in its meshes. A few go further and claim there is also a syncytial relationship between the fibrils of the terminal network and the cells innervated (Stohr,[114, 115, 120] Boeke[121, 122, 123]), or at least that nerve fibrils penetrate into the cells inner-

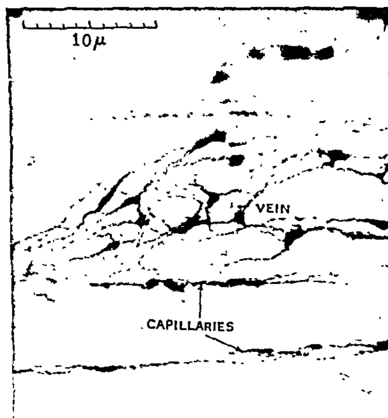


FIG 16

Terminal nerve networks ... vital staining ... structures are almost totally ...

(By courtesy of Professor H A Meyling, Utrecht)

vated This hypothesis has aroused much controversy and its implications are of fundamental interest, for if a terminal autonomic nervous syncytium does exist the neuron theory with its insistence on the anatomical discontinuity of all neurons is not universally applicable. Further, if there really is protoplasmic continuity between the nerve fibrils and the cells innervated—a view less widely held—theories based on chemical mediation across



FIG. 14

Small unpaired ganglion (cranial ganglion impar) in filaments of the opposite internal carotid plexuses extending and meeting alongside the anterior communicating artery of the cerebrum (Rhesus monkey H and E × 130)

FIG. 15

Terminal nerve network around small artery, and fibres from a nerve fascicle *entering* the plexus (Rabbit combined intravital and supravital staining with methylene *blue*)

(By courtesy of Miss E. M. Atkinson, B.Sc. Hons. Anat. Manchester University)

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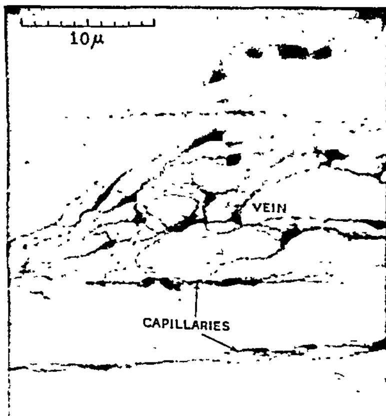


FIG 16

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fictitious junctions between nerve endings and effector cells will require modification or revision.

The idea of a terminal reticulum is much older than is usually stated. The arrangement was described and pictured by Beale[124, 125, 126] in the bladder and around the capillaries of frogs and newts, and similar terminal networks were also noted by His,[127] Holbrook,[128] Berkley [129 A and B] and Von Smirnow.[130]



Fig. 17

Nerve fibril splitting to form a delicate neurofibrillar network around an unstriated muscle cell (Sheep: Bielschowsky-Gros silver impregnation.)
(By courtesy of Professor H. A. Meyling, Utrecht.)

They were also observed by Stirling and Macdonald[131] who termed them *ground plexuses*, a term still used frequently by Continental writers. Probably the profuse networks they saw, especially in viscera, were not entirely nervous, because we know that with their methods of staining reticular and connective tissue fibres may be mistaken for nerve fibres unless controls are employed (Mitchell[132]), but from their diagrams it is almost certain that parts at least of the networks they displayed were nervous. Stirling and Macdonald[131] also noted oval, triangular or irregular swellings at nodes in the networks, which they assumed were ganglion cells. Cajal[113, 133] described these cells as occurring in the fine nerve plexuses supplying the blood vessels, glands and intestines, and regarded them as nervous in nature because they were stained selectively in his Golgi preparations, although he recognised that they were smaller than ordinary ganglion cells. He stated that they contained neurofibrils, that they differed from connective tissue cells and that their processes anastomosed to form a fine nervous network; he called them interstitial cells, but now they are

usually referred to as *autonomic interstitial cells* or the interstitial cells of Cajal Many other investigators (Bethe;[134] Leontowitch;[135] E. Muller;[136] Busch;[137] Okamura;[138] Meyling;[139, 140, 141] Li;[142] Jabonero *et al.*;[143] Jabonero[144, 145, 146]) have agreed with Cajal that these are small ganglion cells, but Dogiel[147, 148] considered they were connective tissue cells, and Lawrentjew[149] suggested they were neurolemmal sheath (Schwann) cells, a view at first adopted by Stohr[150] and Boeke,[151] although they later changed their opinions and regarded them as nervous (Stohr,[119, 120] Boeke[121, 122]). Boeke[121] pointed out that they resemble the small ganglion cells in the enteric plexuses of Amphioxus and suggested that the interstitial cells in mammals are small ganglion cells which have retained their primitive characters. Maximow and Bloom[152] regarded them as probably microglial in nature. Schabadasch,[153, 154] Nonidez,[155, 156, 157] Nageotte,[158] Hillarp[159] and Weddell and Zander[160] believed that they are neurolemmal sheath cells or connective tissue elements, and they denied the existence of a terminal nerve network, believing that the axons run independently and end freely and separately. They regard the networks described by others as artefacts produced by the use of formalin during fixation, but Mitchell[161] has shown that this view is certainly incorrect as the network and cells can be demonstrated in intravital or supravital methylene blue preparations from animals and tissues which have not been treated with formalin at any stage—*e.g* as in all the photomicrographs of terminal networks used in illustrating this section. In these whole thickness preparations the extent of the network can be appreciated only by focusing up and down, and in photomicrographs only parts of the network can be shown in sharp focus, and it will be noted that the constituent fibrils are characteristically beaded or varicose Those who believe in the existence of these terminal networks think that others who claim the nerve fibrils end in pointed or beaded extremities have based their views on imperfectly stained specimens. In methylene blue preparations in particular, unless the fibrils are completely stained they often appear to end freely in pointed or beaded extremities, but in well stained specimens of the same vessels or organs it is seen that there is a true network; and it will be readily appreciated that if parts of the mesh are only partially stained an appearance suggestive of free pointed or beaded endings will result. This appearance may also be reproduced in photomicrographs if the focus is not critical or if, through over- or under-exposure or development, the finest and least evident fibrillae fail to register

The most detailed study of autonomic interstitial cells was published in Dutch by Leeuwe[162] and as Meyling [141] remarks this may explain why so little attention has been paid to his important findings Leeuwe demonstrated by [illegible] Nissl substance which, like [illegible] not dissolved by fat solvents, [illegible] of gastric juice but is readily [illegible]

Feulgen test indicating its nucleine nature. Moreover, just as in sympathetic ganglion cells, the interstitial cells show a positive oxidase and peroxidase reaction. Leeuwe also demonstrated that the interstitial cells differ from sheath (Schwann) cells in staining more easily with methylene blue and in possessing none of the special granules found in sheath cells (Reich[163]); and he claimed further that interstitial and sympathetic ganglion cells differentiate from the

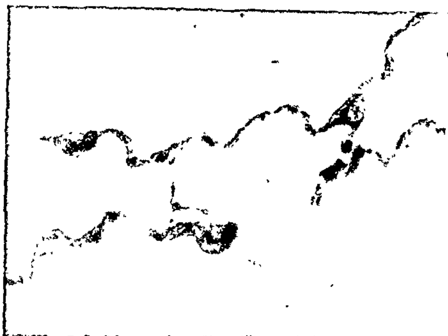


Fig. 18
Autonomic interstitial cells in a vascular terminal nerve network. (Rhesus monkey. intravital methylene blue preparation.)

same neuroblasts. Champy *et al.*[164A and B] have supplied additional proof that autonomic interstitial cells are of a truly nervous nature by using a special stain (osmic acid with sodium iodide) which is said to be specific for diphenols, including adrenalin; this stains interstitial but not connective tissue or sheath cells. Taking all the evidence into consideration there is little doubt that the autonomic interstitial cells are nerve structures. Incidentally, they should not be confused with the larger nerve cells which, as mentioned on p. 25, are sometimes seen lying singly or in small groups alongside certain arteries. The autonomic interstitial cells are delicate, fusiform, star-shaped or pyramidal structures (Figs. 15, 18) with varicose branching processes located at some of the intersections of the meshes of the terminal networks.

The exact significance of the autonomic interstitial cells and terminal networks is still obscure. Most observers believe that the networks are formed by the *terminal fibrils of post-ganglionic sympathetic* and parasympathetic axons anastomosing with the processes of the interstitial cells. Stohr[130] *emphasises that no true endings exist in the* terminal network and that neuro-

fibrils penetrate the protoplasm of the cells innervated. Leeuwe,[162] Meyling,[139] Boeke[121, 122, 123] and Akkeringa[163] believe that the neurofibrillar varicosities in the network represent innervation points, and Meyling[141] states that these enlargements "pass continuously via a periterminal network into the protoplasm of the innervated cells" One has already stressed that if, as seems likely, a terminal nervous reticulum exists, the neuron theory is not universally applicable; and that, if there is protoplasmic continuity between this network and the effector cells, the theory of chemical mediation at hypothetical nerve endings will require modification. Stohr[137] suggests that the chemical mediators are produced in the terminal network and interstitial cells and that the reticulum therefore plays a dual rôle in propagating impulses and producing mediators, and Jabonero[138] expresses somewhat similar views. The site at which adrenalin acts is not exactly known, but it is established as a result of surgical and experimental findings that its effects are still produced after post-ganglionic sympathetic fibres are destroyed, and Dale[140] showed that unstriated muscle cells retain their ability to contract after the administration of ergotoxine although they become unresponsive to adrenaline. As Meyling[141] remarks, this suggests the action of adrenalin must be at some point intermediate between the sympathetic post-ganglionic endings and the effector cells innervated—the position occupied by the interstitial cells—and he postulates that these cells with their anastomosing processes, and not fictitious zones between non-existent nerve endings and the effector cells, are the intermediate structures responsible for chemical mediation. These cells would naturally be influenced by circulating hormones as well as by those produced locally; and in this respect it is significant that by the method of Champy *et al*[164] adrenalin or closely related chemical substances can be demonstrated in some of the interstitial cells and also in the varicosities (Fig 19) of the associated neurofibrillar networks which may represent the innervation points at which the impulse is transmitted to the effector cells. So far there is no similar evidence regarding the possibility that in the interstitial cells connected with the parasympathetic post-ganglionic fibres acetylcholine is produced, but this would be a natural corollary of the above theory

Another group of observations is important. Lawrentjew,[165] Stohr,[166] Meyling[139] and Reiser[167] have demonstrated that the peripheral extensions of the autonomic nervous system do not undergo degeneration after division of the related post-ganglionic fibres, and of the various views propounded to account for this that of Meyling[141] seems to fit the facts best. He suggests that the true terminal networks are formed *only* by the interlacing processes of the autonomic interstitial ganglion cells and that there are synapses between these cells and the post-ganglionic fibres; in this respect, therefore, he departs from the idea that the post-ganglionic fibres are in syncytial continuity with the neurofibrils in the terminal network This conception explains why isolated strips of vessels or intestines separated from their extrinsic nerve supply retain their ability to contract and to respond to chemical and other stimuli; the

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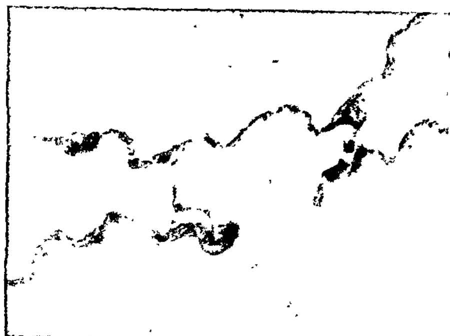


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nerve networks in the amnion and other embryonic tissues. Tinel[174] attached considerable importance to the interstitial cells and pointed out that they are influenced not only by post-ganglionic fibres but also by circulating hormones and physico-chemical changes in the adjoining tissues, so that some degree of local regulation of autonomic function is possible. By such influences the interstitial cells in any locality may become either more or less reactive to impulses reaching them through post-ganglionic fibres, so that these impulses do not necessarily always result in the same response. In effect Tinel claimed, like Meyling, that the sympathetic and parasympathetic fibres do not produce their effects by direct action on the vessels or organs, but through the intermediary of the interstitial cells and terminal networks which are constantly undergoing changes in sensitivity as a result of alterations in their humoral environments

It is customarily stated that groups of unstriated muscle cells are innervated by a single nerve fibre and these functional entities are sometimes referred to as "smooth muscle cell units" or "neuro-effector units." Eccles and Magladery[175A and B] and Fulton and Lutz[176] noted that these units may respond individually to stimulation, *e.g.* the latter investigators succeeded in producing limited vascular responses by stimulating tiny nerves to the blood vessels. Hillarp,[149] on the other hand, thought that several axons end in each neuro-effector unit, with sufficient overlap between adjacent units to explain spreading effects. Cannon and Rosenblueth[177] believed that only some "key" unstriated muscle cells are innervated directly, and that a nerve stimulus reaching them released a chemical mediator which diffused and so activated the adjacent cells. A spreading response, however, is explained equally well, or even better, if one accepts the view that there is syncytial continuity between the processes of the interstitial cells which anastomose to form the terminal networks; these are so all-pervasive that they come into contact with every effector cell The nerve impulses, or hormonal or other humoral changes in the environment of the interstitial cells, lead to the production or liberation of chemical mediators in the cells which spread in decremental fashion through the networks, and depending on the intensity of the impulses the spread may be relatively limited or widespread, with consequent variations in the motor responses

This interpretation of the anatomical arrangement seems to fit the known physiological and pharmacological findings better than any other so far adduced, and it does not conflict with the facts of comparative anatomy, for most observers agree that in the lower forms of life, such as Coelenterates, there is genuine syncytial continuity between the processes of their primitive ganglion cells

A disproportionate amount of space has been devoted to the discussion of this controversial problem because it is of such basic anatomical and physiological importance One last point is worth mentioning. It is difficult to correlate the relative insignificance of the extrinsic vascular nerves with

response is probably neurogenic and not myogenic and due to the persistence of interstitial cells and their anastomising processes which do not degenerate after section of the post-ganglionic fibres; incidentally Esveld[170] showed that intact interstitial cells exist in isolated strips of intestinal wall and on this basis he doubted whether the rhythmic contractions were myogenic. Kuntz[171] argued that they must be myogenic because they persist after the use of



FIG. 19

Beaded fibrils of terminal nerve network between glands in intestinal mucosa, stained by Champy-Coujard technique—a histochemical method for demonstrating adrenaline-like substances

(By courtesy of Professor H. A. Meyling, Utrecht.)

nicotine in amounts sufficient to inhibit synaptic conduction, but clearly this argument is invalidated if the interstitial cells form a syncytium and produce chemical substances which excite plain muscle. Effective peristalsis is abolished by the action of nicotine, because it is a more complicated process than the spontaneous rhythmic contractions of isolated strips of muscle and doubtless depends on the integrity of afferent and efferent pathways containing synapses which are paralysed by nicotine. Fischer[172] believed that he had established that contraction can be purely myogenic because he noted that unstriated muscle cells in the embryonic amnion, which is reputedly devoid of nervous tissue, are inhibited by adrenalin and activated by acetylcholine, but he was obviously unaware that Busch[173] had demonstrated very delicate

Krause types, exist in the adventitia of many vessels or in the immediately adjacent perivascular connective tissue (Hirsch;[186] Woollard;[81] Wilde[87]), especially in those of the extremities (Fig. 20). Afferent nerve endings have

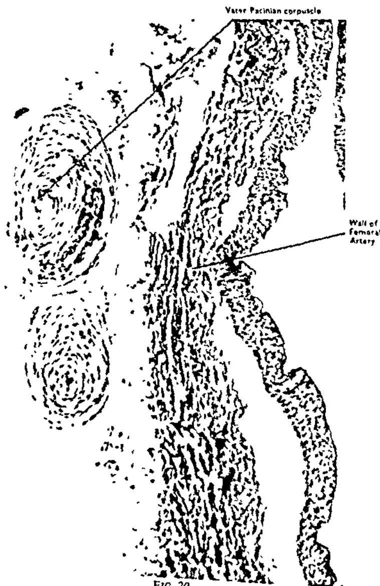


FIG 20

Vater-Pacinian corpuscles in adventitia of femoral artery.

(By courtesy of Mr F. B. Battle, Manchester University, and the Editor and Publishers of the Brit. J. Surg.)

also been described in association with veins (Pereira;[189] de Muylder[187]). Penfield and McNaughton[190] traced sensory fibres from the venous sinuses of the dura mater, but as the walls of these specialised veins are really formed

the apparent profusion of the intrinsic terminal neurofibrillar networks in the vessel walls, but this difficulty vanishes when one appreciates that the latter are accounted for largely by the processes of the numerous interstitial cells rather than by the terminal ramifications of the axons in the vascular nerves.

AUTONOMIC AFFERENTS AND ENDINGS

Gaskell[11] noted the presence of myelinated axons in peripheral autonomic nerves and he, Edgeworth[178] and François-Franck[179A and B] concluded that these fibres transmit visceral and vascular sensations. The Frenchman was far ahead of his time: in discussing the effects of sympathectomy on cardiac and thyroid disease he *surmised that the effects were as much due to suppression* of abnormal afferent impulses to the higher centres in the cord and brain as to the interruption of efferent impulses; and he conjectured that aortic pain afferents were carried in the cervicothoracic and vertebral sympathetic nerves and proposed their division for the relief of angina pectoris—a suggestion that was tried by Jonnesco[180] with reputedly good results, although it is now known that the majority of the cardiac pain afferents run in the thoracic cardiac nerves

Vascular and visceral structures are sensitive to adequate stimuli; and painful, pressoreceptor, chemoreceptor and other centripetal impulses arise in the heart, vessels and other visceral structures, yet many still adhere to the *misconception of the autonomic as a purely efferent system. They claim that* as the fibres carrying visceral sensations pass ultimately through dorsal spinal nerve roots they are really somatic, but with whimsical inconsistence they do not apply such restrictive criteria to the autonomic fibres emerging through ventral spinal nerve roots. Or they say that the pain associated with distending, crushing or ligaturing arteries described by Odermatt,[181] Leriche,[182] Livingston,[183] and familiar to all surgeons, is produced by the accidental involvement of adjacent somatic nerves, or to the *effects of ischaemia resulting* from angiospasm or blockage of the vessels These factors may explain some of the symptoms and signs, but not why a relatively atraumatic procedure, such as piercing an arterial wall with a fine, sharp needle, also produces pain, or why vascular pain sensitivity may persist in areas where other forms of pain sensitivity have been abolished by regional or spinal anaesthesia The truth is, of course, that autonomic afferents exist and are an essential part of the system, and only those who bury their heads in the sands of outworn theories fail to recognize it.

AUTONOMIC AFFERENT ENDINGS

The autonomic afferents convey impressions from endings specially adapted to appreciate pain, stretch, pressure, chemical and other stimuli. Free and spiral endings have been described in the myocardium, and sensory corpuscles of the large lamellated Vater-Pacini type are occasionally seen in the subepicardial tissues and mesenteries (Sheehan[184, 185]). Similar corpuscles and smaller and simpler ones, somewhat resembling the Golgi-Mazzoni or

appear in the media or between the media and intima, or perhaps just beneath the intima or endocardium (Fig. 23). Of course these networks, especially those in the adventitia, are composed of afferent and efferent fibres,

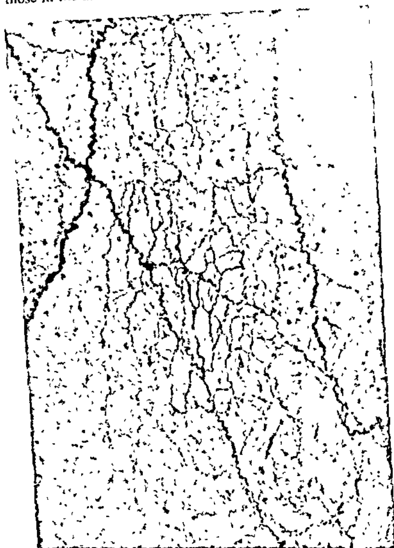


FIG 22
Higher-powered view (× 410) of an area from the same specimen as the one shown in the previous figure.

but in the special receptor areas mentioned the proportion of thicker and presumed afferent fibres is unusually high

Many of the afferent vagal impulses from the heart and aorta are concerned in reflexes that depress cardiac activity and in some animals they are aggregated in a separate component, the *depressor nerve* (Cyon and

by dura mater it is a moot point whether these fibres should be regarded as meningeal or vascular afferents. Masson[111] states that in the neurovascular glomera afferent fibres enter the media from the adventitial plexus to end in small boutons.

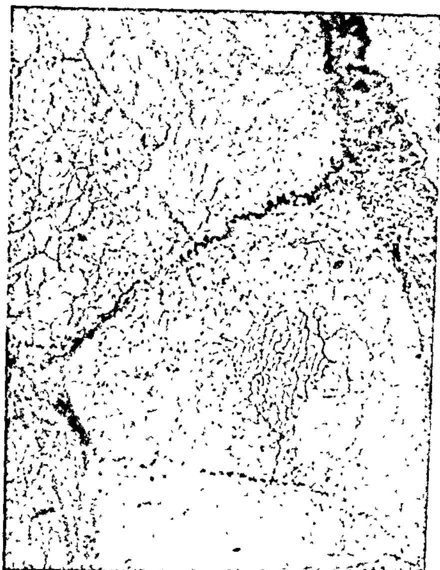


FIG 21

Terminal nerve network in the so-called "depressor area" of the ascending aorta The somewhat H-shaped appearance is produced by larger bundles of nerve fibres (Rhesus monkey combined intravital and supravital staining with methylene blue ×200) *In thick preparations, such as this, it is impossible to get every part in sharp focus in the same microscopic field, a feature evident in several of the photomicrographs*

In the aortic, venacaval, carotid and pulmonary receptor zones there are especially well developed networks of fine varicose fibres, without evident endings (Figs. 21, 22). They are best seen in the adventitia, but finer plexuses

extremities. Thus some of the pain impulses from the limbs or parietes are transmitted through autonomic nerves (Leriche;[192] Fleisch and Weger;[193] Threadgill;[194] Dargent;[195] van Gelderen;[196] Tardieu et Tardieu;[197] Kiaer;[198] Freeman *et al.*[199, 200]). The impulses concerned may originate in the vessels supplying the part. If this is in the proximal part of the limb, *e.g.* the hip joint, most of the fibres involved accompany the blood vessels in paravascular filaments for variable distances before joining branches of the sympathetic trunks, or the trunks themselves, being guided towards the latter by the vessels, which are all derived ultimately from the aorta. If the structure lies more distally in the limb, the paravascular afferents accompany the vessels for variable distances before leaving them to join adjacent cerebrospinal nerves, through which they are then carried to the cord and brain. Generally speaking, in the body cavities and in the head and neck the paravascular nerve pathways are longer than they are in the limbs, although some of the vascular collateral nerves of the extremities are lengthy, such as those accompanying the ulnar and deep femoral arteries. The paravascular pathways explain why in regional anaesthesia the vessels may remain sensitive when other tissues in their vicinity supplied by somatic sensory nerves are insensitive, if the vessels with their paravascular afferents lie outside the anaesthetic area. They also explain the persistence of sensitivity in structures whose surroundings are anaesthetic as a result of spinal anaesthesia; *e.g.* if the level of cutaneous sensory loss does not extend above the tenth thoracic dermatome sensitivity in the testis persists, although its coverings are insensitive, because the afferents involved are carried upwards in the testicular nerves ...

The majority who have studied the problem experimentally or clinically believe that afferent nerve fibres do accompany blood vessels, but there are one or two dissentients; thus Lynn and Simeone[201] failed to confirm the observations of Freeman *et al.*[199, 200] that painful stimuli from the femoral veins in dogs are carried in sympathetic pathways and concluded they must run in cerebrospinal nerves. There is a possible explanation for such discrepancies, especially if the veins are stimulated at different levels. Paravascular filaments can be traced from the superior hypogastric plexus (presacral nerve) alongside the common and external iliac arteries as far as the femoral bifurcation (Mitchell[23, 202]); microscopically they appear to contain both efferent and afferent fibres. As suggested above ...

... afferent stimuli from the proximal and more distal parts of the femoral vessels almost certainly follow different routes as they travel centripetally. White,[203] whose studies on afferent pathways are outstanding, doubts if sympathetic axons are of any importance as an accessory

Ludwig[191]); in man these fibres may run in cardiac filaments of the vagal laryngeal nerves (Mollard[192]).

AUTONOMIC AFFERENT PATHWAYS

It used to be imagined that the cell stations of the peripheral autonomic afferents lay in the ganglia of the sympathetic trunks which were then regarded as reflex centres. These ideas are now discarded and it is believed that the

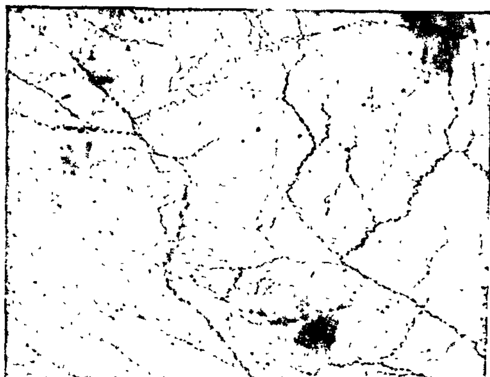


FIG 23

Nerve net [illegible] atrium extending into the commence [illegible] ıbined intravital and supra-vital stain [illegible] ed reflexogenous zone The network ı [illegible] the atrium, and both have [illegible] " depressor area "

dispositions of the afferent visceral neurons resemble fairly closely those of their somatic counterparts. The afferent fibres are the peripheral processes of pseudo-unipolar cells located in dorsal spinal root ganglia or in ganglia associated with the fifth, seventh, ninth and tenth cranial nerves, and they are found both in mixed cerebrospinal and in purely autonomic nerves Those in cerebrospinal nerves carry afferents from vascular and other structures subject to autonomic control in the head and neck, parietes and limbs, and a few (*e.g.* the pudendal nerves) contain afferent fibres both from the parietes and viscera. Conversely autonomic nerves do not carry afferents entirely from vessels and viscera within the body cavities, but may also provide pathways for afferents from structures in the parietes and the proximal parts of the

through the mamillary peduncles and other afferent hypothalamic connections Through relays either in the hypothalamus or thalamus, or in both, some impulses reach cortical levels by neurons corresponding to the third or highest neurons in somatic afferent pathways. Although certain visceral afferent pathways, like their somatic counterparts, may consist of three neurons, others may contain many more linkages (Davis *et al.*[207]). The results of leucotomy and lobotomy operations in man suggest that autonomic pain impulses are conveyed to the frontal cortex; and experimental findings in animals seem to indicate that vagal afferents project to the orbital gyri.

It has also been demonstrated by Downman[208] and Amassian[209,210] in various animals that large fibre elements in the splanchnic nerves project contralaterally to the so-called somatic cortical areas I and II, corresponding with the trunk representation, which are therefore in reality somatovisceral sensory areas. According to Amassian (op. cit.) the fibres concerned run upwards both in the anterolateral and posterior white columns of the cord, and those in the latter relay in the ipsilateral nucleus gracilis, cross in the great sensory decussation in the medulla oblongata, and pass in the contralateral medial lemniscus to the nucleus ventralis posterolateralis of the thalamus Aidar *et al.*[211] found that the impulses with the faster conduction rates run in the posterior white columns (fasciculi gracilis et cuneatus). Other impulses were found to be conducted more slowly through both lateral spinothalamic tracts to the posterior part of the hypothalamus and the caudal portion of the thalamus: these were apparently concerned in the transmission of visceral pain

The probability that autonomic ascending pathways in man are also located in the lateral and anterior white columns is supported by the result of cordotomy operations performed for the relief of intractable visceral pain (White[203]) These produce more or less complete loss of sensation in viscera or vessels whose afferent fibres reach the cord below the level of the operation Incomplete relief is explainable on several anatomical grounds: cordotomy operations are usually limited to the anterior quadrants and do not interrupt the more posterior fibres in the lateral white columns or any visceral afferents which may lie in the posterolateral fasciculi (Lissauer's tracts) or posterior columns (fasciculi gracilis et cuneatus) Moreover as the visceral afferent pathways contain both crossed and uncrossed fibres (Ranson[212]) unilateral sections will not interrupt them completely.

In man the analysis of the referred cutaneous, muscular and vascular signs associated with visceral and vascular disease has been a fertile source of information about the segmental levels in which afferent fibres from these structures end It is commonly believed that abnormal impulses from inflamed, distended or ischaemic viscera transmitted through the primary visceral afferents disturb the common pool of secondary somatic and autonomic neurons in the posterior grey columns of the cord, setting up an

pathway for pain from the upper or lower limbs, but he has no doubt that autonomic, like somatic, nerves play a direct rôle in the transmission of pain.

Vascular afferents from the head structures reach the brain and cord through a variety of pathways. Some run in cranial nerves such as the fifth, seventh, ninth and tenth. These nerves supply direct filaments to many vessels, and they have interconnections with the internal carotid plexus or superior cervical sympathetic ganglion through which some transference of vascular afferents occurs, *e.g.* sensory fibres pass from the carotid plexus to the greater superficial petrosal branch of the facial nerve and so are conveyed to the brain stem (Chorobski and Penfield[204]). Other afferents from the carotid plexus apparently descend through the homolateral sympathetic trunk as far as the upper thoracic region before passing through rami communicantes to the corresponding spinal nerves and so reaching the cord (Altenburger and Kroll[205]); but a proportion may pass into the upper cervical nerves through rami communicantes connecting them with the superior cervical ganglion or the subjacent trunk.

Whether the afferent fibres travel in cerebrospinal or autonomic nerves they are carried ultimately to the central nervous system, the former directly and the latter by being transferred from the sympathetic trunks to cerebrospinal nerves through rami communicantes. They enter the brain or cord through the central processes of the pseudo-unipolar cells located in cranial nerve and dorsal spinal nerve root ganglia. Thereafter some take part in the formation of reflex arcs and others carry impulses to higher autonomic levels—an arrangement resembling that of the lowest neurons in somatic sensory pathways. Those constituting links in spinal reflex arcs form synapses directly, by collaterals, or through intercalary neurons, with cells in the lateral (intermediolateral) or medial (intermediomedial) grey columns. Axon collaterals pass vertically and transversely, so providing the associative and commissural connections requisite for integration, and intercalary neurons perform similar functions. These arcs possess a certain degree of autonomy, but the many subtle vascular and visceral responses essential for normal existence cannot occur after the connections with higher integrating and controlling centres are severed.

Other visceral afferents entering the cord form synapses with cells in the posterior grey columns, or in the adjacent pars intermedia, about their level of entry or a little above it These are the second neurons in the visceral afferent pathways and their fibres decussate in whole or in part and carry the impulses upwards, mainly through tracts in the lateral and anterior white columns of the cord; although in man, as in animals, some may ascend in the posterior or postero-lateral white columns, as White *et al*[206] record that sensations of distension in the bladder and bowel persist after bilateral anterior cordotomies. Their further course and terminations are doubtful, but they probably lie near the lemnisci in the brain stem and some may pass to the thalamus, while others, and perhaps the majority, may reach the hypothalamus

irritable focus (Ross;[213] M'Kenzie;[214] Head;[215] Hinsey and Phillips[216]). In consequence visceral stimuli, which normally are not appreciated, may reach the level of consciousness, and normal thresholds may be altered in such a way that viscerocutaneous, visceromotor and vasomotor reflexes are facilitated. Because the sensorium is normally accustomed to receive the majority of its impulses from parietal structures, when an abnormal number of visceral stimuli arrive at the cerebrum by a psychical misinterpretation they are *referred* to the body surface rather than to the organ affected in which any sensation experienced is relatively dull. Other theories have been adduced to explain these phenomena. Leriche[217] thought that referred pain is mediated through sympathetic and not cerebrospinal pathways, because its location is related to the distribution of the vasomotor nerves rather than to cutaneous spinal nerve root areas. Brown[218, 219] accounts for the pain by assuming that it is interpreted as coming from the position of the affected structure "registered" in the sensorium during development; *e.g.* if the testis (or diaphragm) is the source of painful stimuli, the cerebrum projects the sensation to the site it *believes* the structure still occupies—a psychical misinterpretation referable back to occurrences in utero.

Whatever theory is accepted, they all explain more or less adequately why visceral disturbances may produce painful or other sensations, and why they may be associated with muscular rigidity and vascular phenomena in other areas; and by analysing the physical signs clues are provided to the sites of entry of visceral and vascular afferents and of the segmental levels at which they form synapses within the cord It was by such methods that Head[215] compiled his classical data about the different levels of segmental innervation of various viscera, but he and subsequent observers did not differentiate between visceral and vascular afferents, and doubtless they are too closely associated in most instances to be separated. The majority apparently enter the central nervous system through the dorsal roots of nerves, the ventral roots of which carry the autonomic pre-ganglionic fibres, although it is unlikely that autonomic afferents enter the central nervous system only in the regions corresponding to the putative craniosacral (parasympathetic) and thoracolumbar (sympathetic) outflows. If we attempt to think of visceral afferents in terms of sympathetic and parasympathetic, the comparatively limited distribution of the recognised parasympathetic nerves presents immediate difficulties. This raises the query: assuming parasympathetic afferents exist, are they, like their efferent counterparts, limited to the innervation of certain vascular and visceral structures, or is the current conception of the parasympathetic component altogether too limited? On the efferent side the difficulties associated with limited distribution have been explained away on the basis that vasodilatation in vessels with no acknowledged parasympathetic supply is a negative effect due to diminished sympathetic activity, or, alternatively, that two types of adrenaline-like substance result from sympathetic activity and produce opposite effects. This is feasible, but is it always correct?

For long the intracranial vessels reputedly possessed only a sympathetic supply and dilatation of these vessels was usually regarded as a sequel of diminished sympathethic activity, until Cobb and Finesinger[20] and Chorobski and Penfield[34] showed that at least some of these arteries receive parasympathetic fibres through the facial and vagus nerves. If accepted notions about one set of vessels are found to be incorrect, similar views about the uni-systemic innervation of other visceral structures may also be erroneous. So we return to our question—is our conception too limited, especially in regard to the distribution of parasympathetic nerves? Some observers believe so and have described a widespread vasodilator outflow through the dorsal nerve roots (p. 10). If there is such an outflow, the corresponding afferent inflow could be equally extensive.

INNERVATION OF INDIVIDUAL PERIPHERAL VESSELS

The term " peripheral vessels " is variously interpreted, but here it is held to include all arteries *except* the aorta and those supplying visceral structures. This definition excludes all the vessels within the thorax, abdomen, skull and spinal canal, with a few exceptions such as the internal iliac arteries which supply both visceral and somatic branches. It does not exclude certain arteries which supply viscera located outside the body cavities, *e.g.* the external carotid, which gives off branches to the thyroid and salivary glands.

INNERVATION OF VESSELS IN THE HEAD AND NECK

As stated above, the vessels within the skull and vertebral canal lie outwith the ambit of a survey on peripheral vascular innervation. The arteries supplying the more superficial structures in the head region, such as the face and scalp, receive *parasympathetic* fibres through the facial nerves, and other fibres of similar type are conveyed to vascular and visceral structures in the neck, such as the carotid sinus and the larynx and pharynx, through the glossopharyngeal and vagus nerves this will emerge when the innervation of individual vessels is described. Apart from these, the vessels of the neck, parietes and limbs possess no parasympathetic supply, unless the dorsal root efferent fibres (p 10) really exist: some authorities regard them as the vasodilator supply for the peripheral vessels

The *sympathetic* pre-ganglionic fibres for vessels in the head and neck mainly emerge through the upper two thoracic ventral nerve roots. They reach the sympathetic trunks in white or mixed rami communicantes, relay in the cervical and internal carotid ganglia, and the post-ganglionic fibres are carried in grey or mixed rami communicantes to adjacent cranial and spinal nerves Each ganglion of the sympathetic trunk gives off a number of branches and all contain a varying proportion of vasomotor fibres, so it will be simplest to describe seriatim the ganglia and their branches, commencing with those in the cervical region

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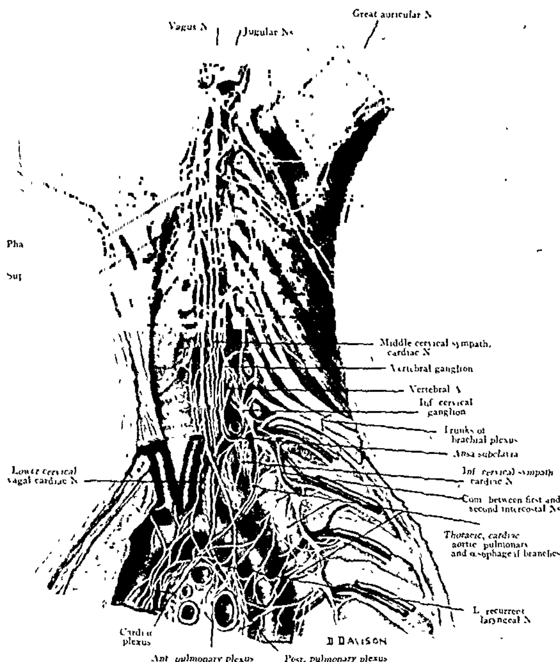


FIG. 24

The cervical and upper thoracic parts of the left sympathetic trunk and their chief branches Other structures such as the left vagus nerve and its branches, the *rami communicantes*, and branches of the spinal nerves, etc, are also visible. In this, as in other drawings, the finer nerve filaments which cannot be seen readily save with the aid of a dissecting microscope are not portrayed

The cervical part of each sympathetic trunk (Fig. 24) extends from the base of the skull to the thoracic inlet, lying posterior to the carotid sheath and anterior to the cervical transverse processes and prevertebral muscles. It is generally said to include three main ganglia—*superior*, *middle* and *inferior*. They are connected by intervening cords, which are usually single, or occasionally double, between the superior and middle ganglia, and often multiple between the middle and inferior ganglia. However, an extra *vertebral ganglion* almost always exists on one of the strands connecting the middle and inferior ganglia; this occurs sufficiently often to describe the normal number as four cervical ganglia. The ganglia receive no white rami communicantes, but they supply grey rami to all the cervical spinal nerves, and also give off communicating rami to several cranial nerves.

The Superior Cervical Ganglion

The superior cervical ganglion is 25 to 45 mm. long and is fusiform, cylindrical, or irregularly constricted (Figs. 24, 25). Rarely it is ovoid or almost globular in shape and if the trunk below it is duplicated the lower pole is bicornuate It lies opposite the first or second to the third or fourth cervical vertebrae, in front of the longus capitis muscle and its fascia, to which it often adheres It lies behind the internal carotid artery, internal jugular vein and glossopharyngeal, vagus, and accessory nerves. The hypoglossal nerve and a plexus of veins lie posterior to its upper pole, and these veins occasionally surround the ganglion in this region

It is formed by the coalescence of three or occasionally four ganglia and it contains synapses between pre-ganglionic and post-ganglionic neurons. The pre-ganglionic fibres mostly emerge in the uppermost thoracic spinal nerves, reach the sympathetic trunk through white or mixed rami communicantes, and then travel upwards through the trunk to the superior cervical ganglion where the majority relay. A relatively small number of fibres may reach the ganglion directly through upper cervical nerve roots, and a proportion of the fibres relay in small ganglia associated with the internal carotid nerves and plexus.

The ganglion receives or gives off communicating, visceral, vascular, muscular, osseous, and articular branches They have also been classified as superior, inferior, anterior, posterior, medial, and lateral, but this classification is largely valueless, *e.g.* the grey rami passing to the cervical and cranial nerves are usually included under the lateral branches, whereas some always arise from other aspects of the ganglion *All these branches*, in addition to those specifically referred to as vascular, *carry vasomotor fibres to vessels in the areas or structures supplied by them*, although naturally they may contain many other fibres which are concerned with secretomotor, pilomotor, sudomotor, pressoreceptor, chemoreceptor and other autonomic activities.

Communicating branches.—The superior cervical ganglion communicates with the last four cranial nerves or with their branches, with the vertebral

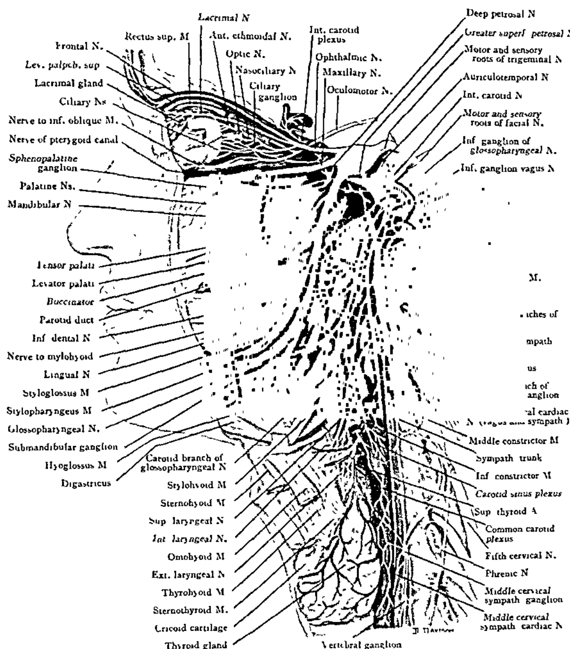


FIG. 25
Lateral view of head and neck showing some of the cranial parasympathetic nerves and ganglia and the cervical portion of the sympathetic system

plexus, and sometimes with the phrenic and descendens cervicalis nerves. It supplies grey rami to the upper three or four, and exceptionally to five, cervical spinal nerves. The post-ganglionic fibres in these communications are distributed, along with the branches of the nerves they join, to vascular and other structures.

Visceral branches.—*Laryngeal* filaments may join the superior laryngeal nerve or its external laryngeal branch directly, but more often they pass through the pharyngeal plexus and so indirectly to the laryngeal nerves; several *pharyngeal* filaments run medial to the internal carotid artery and help to form the pharyngeal plexus. The *superior cervical sympathetic cardiac nerve* originates from the lower part of this ganglion. Other visceral and vasomotor fibres are carried to the salivary, lacrimal, pituitary, thyroid and other glands in perivascular plexuses which are offshoots from the parent vascular nerves and plexuses alongside the carotid arteries.

Vascular branches.—As stated already, *all* sympathetic ganglionic branches contain vasomotor fibres which supply vessels in their areas of distribution, and these fibres are not confined to named vascular branches. The largest of these is the internal carotid nerve, and although the fibres contained in it are mainly distributed to the cerebral and meningeal vessels, a considerable number are also carried to vessels in the eye and orbit and to others in the nose and palate, etc. Part of its course and distribution are therefore described

The **internal carotid nerve** (Fig. 26) is usually single at its origin and appears to be a direct upward continuation of the sympathetic trunk (Mitchell[115, 116]). It arises from the upper pole of the superior cervical ganglion and runs upwards behind the internal carotid artery to enter the carotid canal in the temporal bone About its point of entry into the canal it may divide into medial and lateral branches—Hovelacque[221] states that the point of division is always before the nerve enters the canal, but sometimes the division is within the canal—or the nerve may not bifurcate but continue as a single branch, giving off minute twigs on each side, until it enters the cavernous sinus where it splits into four to six filaments which form a plexus around the artery. Rarely there are two internal carotid nerves *ab initio*, which lie medial and lateral to the artery within the canal

In the carotid canal the branches of the nerve usually break up to form an open-meshed plexus around the artery, within which groups of ganglion cells can be detected microscopically (Fig 13) and one or two may be visible macroscopically (carotid ganglia). These groups of ganglia are more common on the lateral branch, which is the larger of the two. Despite the plexus formation the medial and lateral branches can often be identified as they progress rather sinuously towards the cavernous sinus or they may be lost in the periarterial plexus, although there is a tendency for medial and lateral branches to be reconstituted as the plexus enters the cavernous sinus. These soon split up

again, and the plexus formation is most obvious within the sinus From this plexus subsidiary plexuses are continued along the *hypophysial, cavernous, ophthalmic, meningeal, anterior choroidal* and *cerebral* branches of the internal carotid artery. Microscopic groups of ganglion cells are also present in the cavernous part of the plexus.

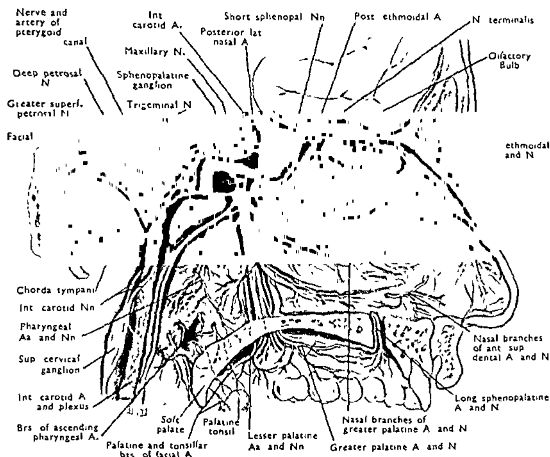


FIG. 26

The internal carotid nerves and some of their branches The sphenopalatine ganglion and its connections and branches, and the vessels and nerves of the lateral wall of the nose, palate and upper pharynx are also shown

Within the lower part of the carotid canal two or more *caroticotympanic* filaments arise from the internal carotid nerve or plexus which pass through canaliculi in the posterolateral wall of the ascending part of the carotid canal to join the tympanic branch of the glossopharyngeal nerve

A deep petrosal filament (Fig. 25) arises from the lateral branch or lateral part of the plexus near the upper end of the carotid canal Emerging from the canal it lies in the fibro-cartilage of the foramen lacerum and soon perforates

this to unite with the *greater superficial petrosal nerve* and form the *nerve of the pterygoid canal.* It forms the so-called *sympathetic root* of the *sphenopalatine ganglion* and is distributed with the orbital, nasal, palatine and pharyngeal branches of this ganglion to vessels and glands in the nose, palate, orbit, etc. The fibres are post-ganglionic and do not relay in the sphenopalatine ganglion: incidentally most of the fibres in the branches of the sphenopalatine ganglion are derived from the ganglionic branches of the maxillary nerve which, though intimately attached to the ganglion, have no functional relationship with it.

In the region of the cavernous sinus the internal carotid plexus communicates with the third, fourth, ophthalmic division of the fifth and sixth cranial nerves, and it may also communicate with the trigeminal ganglion. These communications are variable in size and arrangement, and through them sympathetic post-ganglionic fibres may reach the cranial nerves mentioned

The sympathetic fibres for vessels in the eye and orbit travel for part of their way in the ipsilateral internal carotid nerve and plexus and some may form the so-called *sympathetic root of the ciliary ganglion* (Fig. 25), but this is essentially a parasympathetic relay station and the sympathetic fibres pass straight through it without interruption.

The cervical part of the internal carotid artery, with the exception of its origin, is poorly innervated compared with its other portions within the carotid canal and skull It receives one or two minute nervelets from the superior cervical ganglion, and often additional, but equally insignificant contributions from the nearby superior cervical sympathetic cardiac nerve.

The commencement of each internal carotid artery shows a slight dilatation, the **carotid sinus,** which involves to a minor extent the actual bifurcation of the common carotid artery. These carotid sinuses, and the contiguous carotid bodies, are pressoreceptor and chemoreceptor areas and their particular importance as reflexogenous zones was stressed by Hering[222] and by Heymans *et al.*[223] As in other similar areas, *e.g.* in the [illegible] [illegible] nature. The nerve supply comes both from *parasympathetic* and *sympathetic* sources, but the former is the more abundant. Some observers, such as Boyd,[224] state that a sympathetic supply is relatively infrequent, but one believes that fine sympathetic contributions always reach the carotid sinus [illegible] of its branches. Hovelacque[225] [illegible] ion run to the medial surface [illegible] sinus.

The main supply for the carotid sinus comes from the glossopharyngeal nerve (Fig 25). One or more carotid branchlets arise from the trunk of the parent nerve as it runs across the internal carotid artery, or less often they come from one of its pharyngeal branches: an uncommon source is the nerve

to stylopharyngeus (Boyd[24]). A subsidiary and inconstant supply is derived from the vagus nerve or its superior laryngeal or pharyngeal branches, and the vagal carotid filaments form a loop or loops around the carotid sinus with the corresponding and larger glossopharyngeal branch(es).

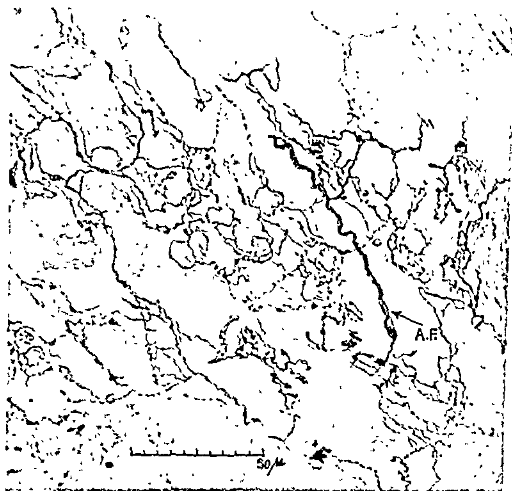


FIG. 27

Sensory terminal nervous network in carotid sinus. A myelinated afferent fibre (AF) is seen to lose its myelin sheath and the termination of the axon is connected with the sensory network. (Horse. vital methylene blue preparation.)

(By courtesy of Professor H. A. Meyling, Utrecht.)

The various carotid sinus nerves end on its walls in forming a perivascular plexus which extends for a short distance on to the adjacent portions of the common and external carotid arteries. Lazorthes[30] thinks that the glossopharyngeal carotid branches mainly supply the carotid sinus and bifurcation, that the sympathetic filaments are distributed chiefly in the external carotid plexus, and that the vagal branches go to the common and internal carotid arteries.

The external carotid and subsidiary plexuses.—The external carotid artery (Fig. 28) and its branches are richly innervated and vasomotor reactions such

as blushing or blanching are often conspicuous in their territories of supply. Four to six filaments from the anterior aspect of the superior cervical sympathetic ganglion reach the first 2 - 3 cm. of the main vessel, and they are often

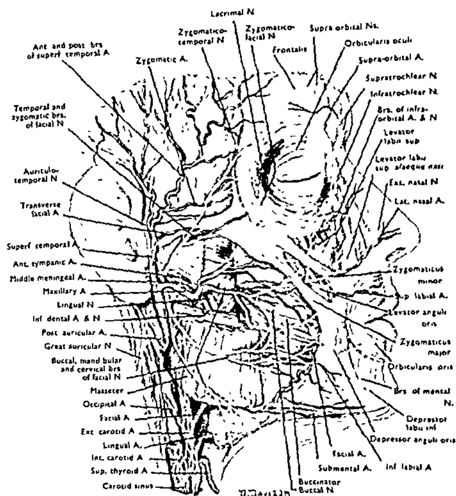


FIG. 28

conjoined in parts of their courses with carotid sinus and internal carotid filaments They divide and subdivide, forming a plexus around the artery. Each branch of the artery is surrounded by a subsidiary plexus derived from the main plexus, which is most conspicuous around the lowest part of the artery, particularly near the origin of its facial branch. This area has been

described as a reflexogenous zone analogous to, but less important than, the carotid sinus, and Lazorthes[76] states that a small "*facial ganglion*" often exists in the plexus just below the origin of the facial artery; it should not be confused with the *facial ganglion* situated on the genu of the seventh cranial nerve. Another small ganglion is sometimes found close to the origin of the posterior auricular artery, and occasionally a filament from the seventh cranial nerve joins the external carotid plexus about the same level: it is uncertain whether this ganglion is sympathetic or parasympathetic, but it may be a relay centre for parasympathetic vasodilator and secretomotor fibres derived from the seventh or ninth cranial nerves.

Apart from an inconstant contribution from the facial nerve, the part of the external carotid artery within the parotid gland receives no branches, but the terminal part of the vascular plexus is reinforced by two or three filaments from the auriculotemporal nerve and by one or two strands from the facial nerve.

The chief branches of the external carotid artery are *superior thyroid, lingual, facial, ascending pharyngeal, occipital, posterior auricular, superficial temporal* and *maxillary*. All are surrounded to a variable degree by subsidiary nerve plexuses derived from the parent plexus on the main vessel, and all are supplied by additional filaments from adjacent cerebrospinal nerves.

The superior thyroid arterial plexus, derived from the parent external carotid plexus, receives inconstant additional filaments from various sources such as the superior cervical ganglion or its superior cardiac branch Less often very fine branches reach it from the superior laryngeal nerve or from the nervus descendens hypoglossi.

The **lingual** arterial plexus, continued from the main plexus, is reinforced by filaments from the lingual and hypoglossal nerves (Hirschfeld[225]) or perhaps from the superior laryngeal nerve (Delmas and Laux[226]).

The **facial** arterial plexus is especially rich and may contain a small ganglion at its origin from the main external carotid plexus. Most of the filaments from the superior cervical ganglion to the external carotid plexus reach it about the level of origin of the facial artery Hirschfeld[225] noted that the subsidiary plexus continued on the submental branch of the facial artery may carry the sympathetic root of the submandibular ganglion, or this root is derived from the facial plexus itself Reinforcing filaments join the plexus from the cervical or mandibular divisions of the facial nerve, from the mental nerve and from the nasal branches of the infraorbital nerve

The **ascending pharyngeal** plexus is inconspicuous and fine interconnections exist between it and the pharyngeal plexus

The ***posterior* auricular** plexus is also inconspicuous It receives a reinforcing filament from the corresponding branch of the facial nerve

The **superficial temporal** artery is one of the two terminal branches of the external cartoid artery. The nerve plexus around it is well defined, and near

its commencement a filament reaches it from the auriculotemporal nerve. The transverse facial, zygomatic, anterior (frontal) and middle temporal branches receive additional filaments from the temporal and zygomatic branches of the facial nerve, from the supra-orbital branch of the frontal nerve, from the zygomatic branch of the maxillary nerve, and from the auriculotemporal branch of the mandibular nerve. The plexus around the posterior (*parieto-occipital*) branch of the *superficial temporal* artery is joined by one or more filaments from the greater occipital nerve.

The **maxillary** artery is the larger terminal branch of the external carotid artery and the greater part of the termination of the external carotid vascular plexus is continued along it. In turn the middle meningeal branch of the maxillary artery carries off a disproportionate share of the plexus, and the nerve fibres accompanying it are distributed to the meninges and their vessels in the middle meningeal territory of supply. This meningeal plexus gives off the sympathetic root of the otic ganglion, receives twigs from the auriculotemporal nerve loop surrounding the artery, and is joined by other twigs from the nervous spinosus.

The main part of the *maxillary arterial* plexus is reinforced by fine contributions from the facial nerve or its temporal branch, from the auriculotemporal, buccal or inferior dental branches of the mandibular nerve, from the sphenopalatine ganglion, and from the posterior superior dental branch of the maxillary nerve.

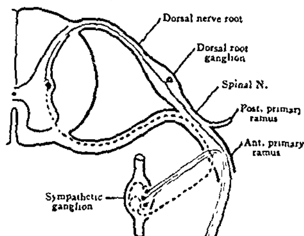
The veins.—The veins of the head and neck have a relatively meagre nerve supply in comparison with most of the arteries and it is often difficult to detect where nerve filaments actually join them, although nerve fibres can be detected in their walls on microscopic examination Hovelacque[221] described a branch of the buccal nerve passing to the *facial vein*. Other filaments supplying the *internal jugular vein* are more easily detected. They come from the upper end of the superior cervical sympathetic ganglion (Fig. 24), and sometimes a tiny twig is supplied by the vagus or hypoglossal nerves. They end around the superior jugular bulb, but many may carry afferent meningeal fibres from the posterior cranial fossa.

Osseous, articular and muscular branches.—These are supplied by the superior cervical as well as by other ganglia of the sympathetic trunks, and most of the information given below, with a few obvious exceptions, is generally applicable and will not be repeated subsequently.

By microdissection methods, and in decalcified and stained specimens, it is possible to detect fine strands from any of the sympathetic trunk ganglia or rami communicantes entering adjacent vertebrae, intervertebral discs, joints, and voluntary muscles Many accompany minute vessels and supply them, and others may be sensory. Jung and Brunschwig[227] and Roofe[228] have demonstrated unmyelinated nerve fibres and sensory endings in the intervertebral disks, but many of these are probably derived from the small recurrent menin-

geal branches of the spinal nerves. A proportion of the fibres in these recurrent branches are post-ganglionic fibres from the *neighbouring* sympathetic trunk or from intermediate ganglia.

The fibres entering voluntary muscles from rami communicantes are not *always entirely autonomic*; in certain regions somatic fibres from the spinal nerves run along the grey rami for variable distances and then leave them to enter the prevertebral muscles. However, the majority of *the fibres entering the prevertebral* and paravertebral muscles from these sources are sympathetic. Compared with most cutaneous vessels, *muscular arteries have a beggarly innervation* (Clark[229]). The sympathetic fibres for cutaneous structures are *carried in the somatic nerves innervating* the parts (Fig. 29).



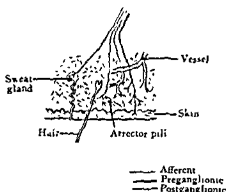


Fig. 29

Distribution of sympathetic post-ganglionic fibres (blue) through a spinal nerve to skin structures such as vessels, sweat glands and arrectores *pilorum*.

The Middle Cervical Ganglion

This ganglion is small (Fig. 24) and inconstant and cannot be recognised as a distinct entity in 20 to 25 *per cent. of subjects*, although in such cases several minute nodules usually exist in the sympathetic trunk above, below, or at the same level as that normally occupied by the middle ganglion. This ganglion, *or* [illegible] *fuse* [illegible] and sometimes it may include the *whole or parts of the fourth or* seventh. Like the superior cervical ganglion it often adheres to the fascia over the prevertebral muscles.

When a single ganglion exists it usually lies anterior to the interspace between the transverse processes of the fifth and sixth cervical vertebrae, just above or in front of the inferior thyroid artery, or less often behind this vessel It varies in shape, being fusiform, rounded, waisted, or star-shaped. When groups of tiny ganglia are present they lie both above and below the level of the inferior thyroid artery, and are often interconnected by three to four very thin cords passing *both anterior and posterior to the vessel*.

The trunk between the superior and middle ganglia is more often single than double, but below the ganglion the trunk is *seldom or never single* In

over a hundred foetal and adult subjects in which this particular feature has been studied, a single trunk in this situation was never seen. In the simplest [illegible] ...medial one forms a loop, the [illegible] he subclavian artery, lying in [illegible] (Sibson's fascia); the postero-lateral cord often splits to enclose the vertebral artery before passing to the inferior cervical ganglion, or it gives off side branches which loop around the vessels. A *vertebral ganglion* is often present on one or other of these cords, but if this ganglion lies above the artery, the trunk between it and the middle ganglion may be single. Below the vertebral ganglion the trunk usually breaks up into six to eight filaments which form loops around both the subclavian and vertebral arteries before joining the inferior cervical ganglion. There are numerous variants of the above arrangements, but it would be tedious and pointless to catalogue them all.

The middle ganglion receives or gives off communicating, visceral, vascular, osseous, muscular, and articular branches.

Communicating branches.—It contributes grey rami communicantes to the fifth and sixth and sometimes also to the fourth or, rarely, to the seventh cervical spinal nerves. It sends one or two filaments to the vertebral plexus, and occasionally direct connections exist between it and the vagus, phrenic, *and recurrent laryngeal nerves. The post-ganglionic* fibres reaching the spinal nerves are distributed with them to vessels and other structures in their areas of supply.

Visceral branches.—Visceral branches are supplied to the thyroid and parathyroid glands, to the trachea and oesophagus, and to the heart.

Vascular branches.—These help to innervate the *common carotid, vertebral* and *inferior thyroid* arteries, and perhaps the jugular veins. The innervation of the vertebral artery will be described along with the vertebral ganglion and nerves, and the nerve supply of the inferior thyroid artery along with that of the subclavian *artery*.

The **common carotid** artery receives few vascular filaments and its perivascular plexus is not rich, except at its termination where it *shares in the* profuse supply of the carotid sinus. The fine common carotid *nervelets* usually come directly from the middle cervical ganglion or the immediately adjacent part of the trunk Hovelacque[33] found that occasional filaments reached it from the superior cervical sympathetic cardiac nerve, but as this *nerve often unites not far below* its origin with a corresponding branch from the vagus, the vascular fibres could come either from the superior cervical ganglion or from the vagus.

***Muscular*, osseous, and articular branches.**—These were described in general terms on page 53.

The Vertebral Ganglion

A small ganglion (Figs. 24, 25, 30) is almost constantly found on one or other of the cords interconnecting the middle and inferior cervical ganglia and the most common situation is anterior to the vertebral artery near its point of entry into the foramen transversarium of the sixth cervical vertebra. Less often it lies just above and slightly anterior to the artery, or lateral to the vessel. If two ganglia exist in this situation, one usually lies anterior to the vertebral artery and in direct contact with it, and the other may be anteromedial or anterolateral to it. The trunk connecting it to the middle ganglion may be single, but invariably several cords exist between it and the inferior ganglion and one, or more often two, of these form the *ansa subclavia*. Jonnesco,[180] Hovelacque[221] and others referred to this as the " ganglion intermédiaire," but the term " vertebral ganglion " is preferable because it is related to and helps to supply the vertebral artery, and because the term intermediate ganglion (p. 14) is now invariably applied to ganglia on the rami communicantes or ventral nerve roots. Lazorthes and Cassan[231] suggested that the vertebral and stellate ganglia should be described together as the " cervicothoracic ganglion," but this term is more properly applied to the stellate ganglion which is truly cervicothoracic, whereas the vertebral ganglion is entirely cervical and in the majority of cases is a separate structure.

It is connected most often by rami communicantes to the sixth and/or seventh cervical spinal nerves and so represents a lower detached element of the middle cervical ganglion or an upper detached portion of the inferior cervical ganglion. However, it is almost constantly found and there is reason to regard it as a normal fourth ganglion in the cervical chain. It does not vary inversely in size with the middle and inferior ganglia, and this strengthens its claim to consideration as a normal constituent of the cervical series and not merely as a detached element of the other ganglia.

Its communicating rami with the spinal nerves and its involvement in loops around the subclavian and vertebral arteries have been mentioned. It may also communicate with the phrenic and vagus nerves, and it supplies thyroid, oesophageal and tracheal filaments. Occasionally the middle cervical cardiac nerve arises from it, or it supplies one or two rootlets to this nerve

The vertebral nerves.—The vertebral ganglion invariably supplies a branch (or branches) which runs up on the anterior or anterolateral aspect of the vertebral artery (Fig 30); in two subjects with no vertebral ganglia this branch arose from the middle cervical ganglion. Another, and usually larger, vertebral nerve arises from the inferior cervical or stellate ganglion and ascends posterior to the artery. The former may arise from the vertebral ansa associated with the vertebral ganglion, and the latter may originate from the subclavian ansa which is connected to both the vertebral and stellate ganglia Both anterior and posterior vertebral nerves often arise by two or three fine rootlets. As they pass upwards through the foramina transversaria they com-

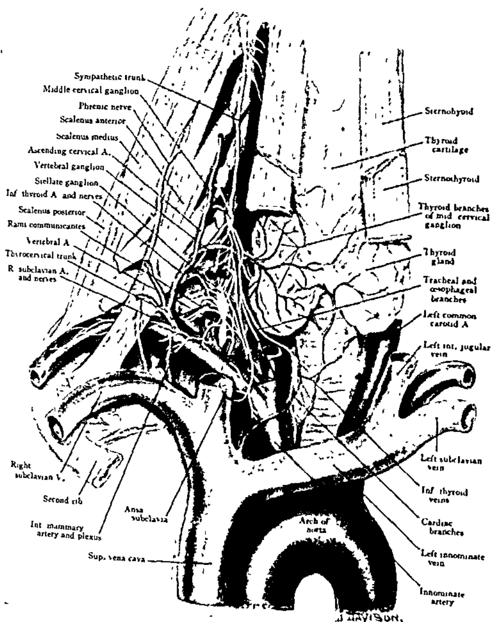


Fig. 30

Root of neck, showing the middle cervical, vertebral and stellate ganglia, the ansa subclavia, vascular subclavian filaments from the stellate ganglion, etc

municate by oblique branches forming an open periarterial plexus, and this is often reinforced by filaments from the superior and middle cervical ganglia which run backwards between the cervical transverse processes. Besides their vascular branches, they also supply filaments to the adjacent vertebrae, discs, and meninges, although the fibres innervating these structures often join the recurrent meningeal branches of the upper five or six cervical nerves and are distributed with them. The posterior part of the vertebral plexus supplies deep rami communicantes to the upper five or six cervical spinal nerves as these nerves run outwards between the transverse processes immediately posterior to the vertebral artery and its plexus. These rami from the vertebral nerves provide an unusually deep series of efferent and afferent pathways. In its cervical course several small collections of ganglion cells are present in the vertebral plexus or on the posterior vertebral nerve. Within the cranium the plexus is continued on the vertebral and basilar arteries and sends subsidiary plexuses along their various branches.

The vertebral nerves are interesting structures and their true nature is still in doubt. They have been variously regarded as a deep cervical sympathetic chain (Valentin,[86] Guerrier[232]), as a form of splanchnic nerve carrying accelerator and sensory cardiac fibres (François Franck[179A and B]), and as deep rami communicantes conveying post-ganglionic and afferent fibres to and from upper cervical spinal nerves (Hovelacque[221]); but whatever else they may be, all are agreed that a proportion at least of their fibres innervate the vertebral artery.

Laux and Guerrier[233] divided the innervation of the **vertebral artery** into three segments—an inferior from the anastomoses between the anterior and posterior vertebral nerves described above, a middle by a filament from the middle cervical ganglion, and a superior by twigs from the third cervical nerve and from the loop uniting the anterior primary rami of the first and second cervical nerves in front of the atlas This loop communicates with the superior cervical sympathetic ganglion and with the vagus and hypoglossal nerves. Lazorthes[36] distinguished two segments of innervation; the longer vertical part extending from the origin of the artery almost to the level of the axis is supplied by the anterior and posterior vertebral nerves arising respectively from the vertebral and stellate ganglia; and the sinuous part preceding the entrance of the artery into the skull which is supplied by filaments from the first and second cervical nerves or from the loop interconnecting them. The vascular twigs arise from the loop close to the point where it is joined by a communicating ramus from the superior cervical ganglion, but Lazorthes found that vascular contributions from the vagus, accessory or hypoglossal nerves to the vertebral artery are very inconstant Apparently the part of the vertebral perivascular plexus entering the skull is provided mainly or entirely by the twigs reaching the sinuous arterial segment, because the lower part of the plexus formed by the vertebral nerves gradually fades out as the artery ascends through the foramina transversaria

The Inferior Cervical Ganglion: Stellate or Cervicothoracic Ganglion

This ganglion corresponds to the seventh and eighth cervical ganglia, and in 75 - 80 per cent. of subjects it is partly or completely fused with the first or even the second thoracic ganglion (ganglia) to constitute a stellate ganglion (Figs 24, 30, 35). As this is the commonest arrangement it will be selected for description.

The stellate ganglion in life has a creamy-pink colour similar to that of the adjacent arteries, and it is intermediate in size between the superior and middle cervical ganglia, being shorter and broader than the former. It varies in length between 1·5 to 2·5 cm. and is about 0·5 to 0·75 cm. wide at its broadest point. It is irregular in shape, having a waist or being irregularly constricted, and it derives its name from the appearance presented by its numerous radiating branches. It lies anterior to the last cervical transverse process, the neck of the first rib, and the anterior primary ramus of the eighth cervical nerve as it passes outwards to unite with the corresponding division of the first thoracic nerve. It overlaps the lateral margin of the longus cervicis and its covering fascia, to which it is attached, or it is just outside the line of the muscle. As it rests on the neck of the first rib it is medial to the superior intercostal artery and its vena comitans; immediately lateral to these vessels is the anterior primary ramus of the first thoracic nerve passing upwards and outwards to the brachial plexus It is located posterior to, but not in direct contact with, the first part of the subclavian artery and the origin of the vertebral artery, and these vessels separate it from the main vertebral vein, which emerges through the foramen transversarium of the sixth cervical vertebra, the vertebral vessels lie closest to the ganglion at its superior pole and may actually indent it A small accessory vertebral vein sometimes descends from the venous plexus around the vertebral artery and issues through the transverse foramen of the seventh cervical vertebra to pass forwards between the ganglion, the dome of the pleura, and the subclavian artery to join the innominate vein The ganglion also lies posterior to the apex of the lung, but separated from it by the pleura and the suprapleural membrane, and in embalmed cadavers it produces a shallow impression in these structures. A musculo-aponeurotic slip derived from the scalene muscles near their vertebral attachments spreads out as it passes downwards to become attached to the suprapleural membrane, and in approaching the ganglion from the front this thin sheet may veil the stellate ganglion more or less completely. The scalenus minimus is another inconstant anterior relation; it runs from the seventh cervical transverse process to the inner border of the first rib, and Telford and Mottershead[24] found it is present in about one in three subjects. The costocervical trunk, the internal mammary, inferior thyroid and common carotid arteries, the vagus and phrenic nerves, and the internal jugular and innominate veins are all indirect anterior relations, although the costocervical

trunk, or rather its superior intercostal branch as it curves backwards to the neck of the first rib, intervenes between the ganglion and the suprapleural membrane. The right lymphatic duct and the thoracic duct on the left side are also indirect anterior relations, and they are surrounded by plexuses of small veins which may prove troublesome to a surgeon approaching the ganglion from the front.

The arrangement of the connections between the middle, vertebral and stellate ganglia have been described, but a few additional details about the **ansa subclavia** (Figs. 24, 30) are desirable. This loop passes in front of the first part of the subclavian artery and curves up behind it to join the stellate ganglion. The ansa is seldom single and usually consists of two or more filaments of varying size. The upper ends of the filaments are attached to the middle cervical or vertebral ganglia, or both, or to interganglionic parts of the trunk, and the lower ends may be attached at any point between the upper and lower poles of the stellate ganglion. It is not unusual to find a periarterial loop which is attached at both ends to this ganglion, and rarely corniculate processes project from the ganglion and partially embrace the artery at their ventral ends. Any of the ganglionic branches may arise from the ansa, and it appears to be constantly connected to the homolateral phrenic nerve by elongated filaments.

The stellate ganglion receives or supplies communicating, visceral, and vascular branches and gives off the usual filaments to locomotor structures.

Communicating branches.—The stellate ganglion receives one or more white rami communicantes from the first and occasionally from the second thoracic nerves, and mixed rami may also be connected to it. Kuntz[92] demonstrated that the first and second and sometimes the second and third (Kirgis and Kuntz[93]) anterior primary rami of the thoracic nerves are interconnected by inconstant vertical branches which lie in front of the necks of the corresponding ribs lateral to the main sympathetic trunk; they contain post-ganglionic fibres derived from grey rami connected with these nerves. When these branches are present they provide alternative channels through which sympathetic post-ganglionic fibres may reach the first thoracic nerve and the brachial plexus, and possibly some pre-ganglionic fibres also run through them from the second or third thoracic nerves to the stellate ganglion

The ganglion sends grey rami communicantes to the eighth cervical and first thoracic nerves, occasionally to the seventh cervical and second thoracic nerves, and rarely to the sixth cervical nerve. These rami vary in number between one to six per nerve and convey efferent and afferent sympathetic fibres to and from the brachial plexus They help to innervate vessels, sweat glands, arrectores pilorum and locomotor structures in the extensive area supplied by the branches of the brachial plexus. The ganglion or the ansa subclavia invariably communicate with the homolateral phrenic nerve, and almost constantly with the vagus nerve or its recurrent laryngeal branch

Shaw[225] stated that the fibres joining the vagus and recurrent laryngeal nerves are distributed ultimately to the heart, oesophagus, and larynx. Fine direct interconnections may exist between the stellate ganglia of opposite sides, although they are very uncommon.

Visceral branches.—All these contain a proportion of vasomotor fibres, and branches are supplied to the heart, trachea, and oesophagus. Other filaments enter the suprapleural membrane and have occasionally been traced through it into the dome of the parietal pleura. In infants twigs from this ganglion or from the *ansa subclavia enter the thymus.*

Vascular branches.—The vascular branches of the stellate ganglion are more interesting than most from the clinical angle, because many of them are concerned in the innervation of the vessels of the upper limb. The levels of representation in the spinal cord (p. 8) and of the outflows of pre-ganglionic fibres (p 9) have already been discussed, and the arrangement and distribution of the post-ganglionic fibres have also been described in a general way (p. 18) Now it remains to give more details about the innervation of individual vessels

INNERVATION OF VESSELS OF UPPER LIMB

The subclavian artery (Fig. 30).—Wrisberg,[226] Arnold,[227] Bourgery,[228] Hirschfeld[229] and many subsequent observers noted vascular filaments passing directly from the inferior cervical or stellate ganglion to the proximal part of the subclavian artery Kramer and Todd[82] described additional branches arising from the ansa subclavia and occasionally from the middle cervical ganglion, and Hovelacque[230] added the information that yet other subclavian filaments might arise from the vertebral ganglion (ganglion intermédiaire). Delmas and Laux[231] and Lazorthes and Cassan[232] expressed similar views. There was, and is, uncertainty about how far the direct vascular filaments from the ganglia or ansa may extend, but apart from a few such as Hirschfeld[229] who claimed that he could follow them as far as the brachial artery, most agree that they extend no further than the subclavian-axillary junction. The arterial stem of the upper limb and its branches beyond this level *are supplied by vascular filaments* derived from adjacent mixed spinal nerves (Kramer and Todd[82]; Woollard[40]).

The number of filaments (two to six) arising from the stellate ganglion and the ansa subclavia is variable, and the size is in inverse proportion to the number The supply from the vertebral ganglion is inconstant, and when present it usually joins the subclavian artery close to the origin of its thyrocervical branch Inconstant nervelets may also join the perivascular plexus from the cervical sympathetic cardiac nerves (especially the inferior), and the third or terminal part of the artery usually receives delicate twigs from the lowest trunk of the brachial plexus

The branches of the subclavian artery are the vertebral and internal mammary arteries and the thyrocervical and costocervical trunks All are surrounded by subsidiary perivascular networks derived from the nerve plexus around the parent vessel.

The **vertebral** nerves and plexuses were described along with the vertebral ganglion (p. 56).

The **internal mammary** artery is surounded by offsets from the main subclavian plexus and may also receive direct filaments from the ansa subclavia or vertebral ganglion. In turn the internal mammary plexus gives small subsidiary plexuses which surround its various branches, such as the anterior intercostal, sternal, perforating, musculophrenic and superior epigastric arteries.

The **thyrocervical trunk** is short, dividing almost immediately into inferior thyroid, suprascapular and transverse cervical arteries.

The *inferior thyroid* arterial plexus receives filaments from the main subclavian plexus and it is usually reinforced by twigs from the vertebral and middle cervical ganglia. It may communicate with the homolateral recurrent laryngeal nerve and sometimes small ganglia are said to exist within it. It has been suggested (Lazorthes[56]) that the middle cervical ganglion represents the vasomotor centre for the arteries in the pharynx, larynx and thyroid gland; and that the minor plexus around the ascending cervical branch of the inferior thyroid artery is a subsidiary cervical sympathetic trunk (Guerrier[232]).

The *suprascapular* and *transverse cervical* arteries are innervated by continuations from the main subclavian plexus. From an anastomosis between the middle cervical ganglion and the phrenic nerve fine offshoots pass to the transverse cervical artery.

The **costocervical trunk** divides into the superior intercostal and deep cervical arteries and both the trunk and its branches are innervated by filaments from the main subclavian plexus.

The *superior intercostal* artery crosses the neck of the first rib just lateral to the sympathetic trunk and it always receives a twig or twigs from the stellate ganglion, or from the first thoracic ganglion when the latter is not fused with the inferior cervical ganglion This vessel usually supplies the first two posterior intercostal arteries.

The *deep cervical* artery is analogous to the posterior branch of a posterior intercostal artery and may receive a filament from the eighth cervical nerve as it passes backwards above it between the transverse process of the last cervical vertebra and the neck of the first rib.

The axillary artery (Fig. 31).—Hirschfield,[225] Kramer and Todd[82] and Hirsch[186] all believed that the first part of this artery is innervated by an extension of the fibres on the subclavian artery which reach that vessel directly from the sympathetic trunk, and it is now generally agreed that this form of direct sympathetic innervation extends at least to the subclavian-axillary junction. Beyond this level the artery receives sympathetic fibres which have

ırsued an indirect route through grey rami communicantes to the brachial exus and then from the plexus or its branches to the artery. The plexus ·ound the upper half of the artery is augmented by filaments from the medial ıd lateral cords of the brachial plexus which reach the posterior or postero-

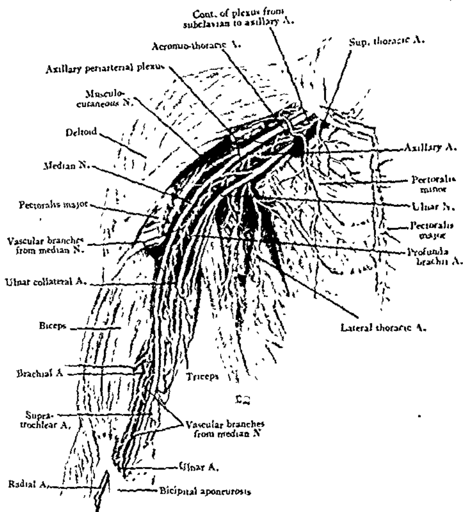


Fig. 31

The axillary and brachial arteries with their main branches, periarterial plexuses and reinforcing vascular nerves

lateral surface of the vessel, and another filament may be supplied by the loop interconnecting the medial and lateral pectoral nerves. The lower half of the vessel receives one or two fairly substantial strands from the median nerve Rarely one has noted very fine bundles of fibres passing from the median nerve to the axillary vein.

All the arterial branches—*superior thoracic, acromiothoracic, lateral thoracic, subscapular, circumflex scapular,* and *anterior and posterior humeral circumflex*—are innervated by filaments derived from the main axillary peri-

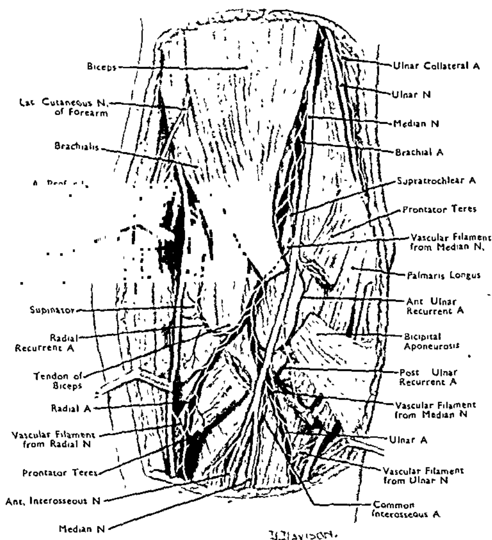


FIG. 32
The distal part of the brachial artery and the proximal parts of the radial and ulnar arteries with their main branches and vascular nerves

vascular plexus, and they may also receive twigs from adjacent nerves, *e g* the circumflex humeral arteries from the circumflex nerve

The brachial artery (Figs. 31, 32).—As the direct continuation of the axillary artery, this vessel carries a prolongation of the axillary plexus, and it is

reinforced at intervals between the axilla and elbow by 3 or 4 filaments from the median nerve. These were noted by Klint[210] and by many subsequent observers. Kramer and Todd[12] claimed that the musculocutaneous nerve also supplies the artery, but *this supply is inconstant.* Hirsch[100] stated that the upper part is supplied by the radial (musculospiral) nerve and the lower part by the median, with the musculocutaneous and ulnar nerves as rare additional or alternative sources of supply.

The median filaments as the most constant and important, and the lowest and largest one, *which arises within* 1 - 3 inches (2·5 - 7·5 cm.) of the elbow joint, joins the artery not very far above its bifurcation. It divides with the artery into halves which follow the course of the radial and ulnar arteries.

The *profunda brachii, nutrient, ulnar collateral, muscular* and *supratrochlear* branches of the brachial artery all receive offsets from the plexus around the *main vessel* The profunda brachii obtains a supplementary supply from the radial nerve and the ulnar collateral artery gains one or two twigs from the ulnar nerve.

The plexuses are distinct on the arteries forming the anastomosis around the elbow joint, and in this respect they conform to the general rule that *articular and periarticular arteries are relatively* well supplied with nerves (p 19).

The ulnar artery (Figs. 32, 33).—The *initial* part of this vessel is supplied by a continuation of part of the brachial plexus, including part of the median nerve filament which runs to the termination of the brachial artery. Below *this level the* ulnar artery is innervated *by a long, slender branch of the ulnar* nerve (Henle[241]) which can often be traced to the point where the artery gives off its deep branch immediately beyond the pisiform bone. This ulnar arterial nerve, which is occasionally replaced by several twigs, gives offsets to the various branches of the ulnar artery, and some of these branches also *receive nerve filaments from other sources.* Thus the *anterior and posterior ulnar recurrent* arteries gain a supply from the median (or its branch to pronator teres) and ulnar nerves respectively, and the *anterior and posterior interosseous* arteries get additional filaments from the corresponding nerves *which are branches of the* median and radial nerves respectively.

The radial artery (Figs. 32, 33).—The first part is supplied by a prolongation of the brachial perivascular plexus and by one of the subdivisions of the median nerve filament which runs to the termination *of the brachial artery.* Lower down the plexus is reinforced by two or three frail bundles from the radial nerve As usual the arterial branches are innervated by extensions from the plexus on the *main vessel, sometimes* supplemented by filaments from adjacent nerves For example the *radial recurrent artery* receives extra twigs from the radial nerve and its posterior interosseous branch

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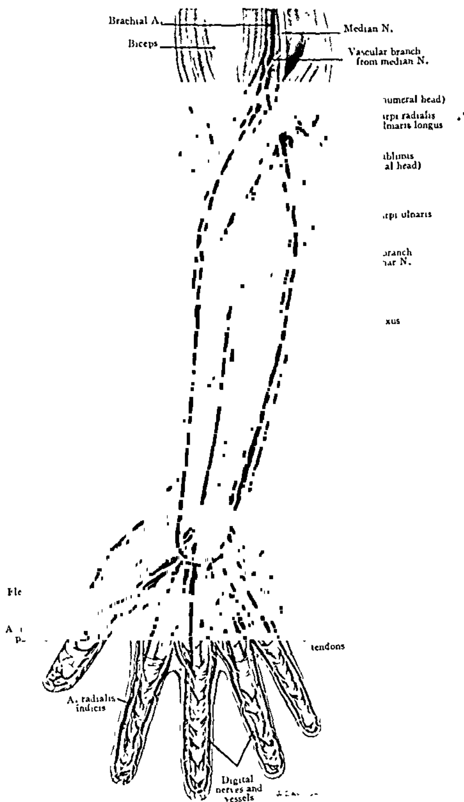


FIG. 33
Radial, ulnar and palmar arteries, with their nerve supplies

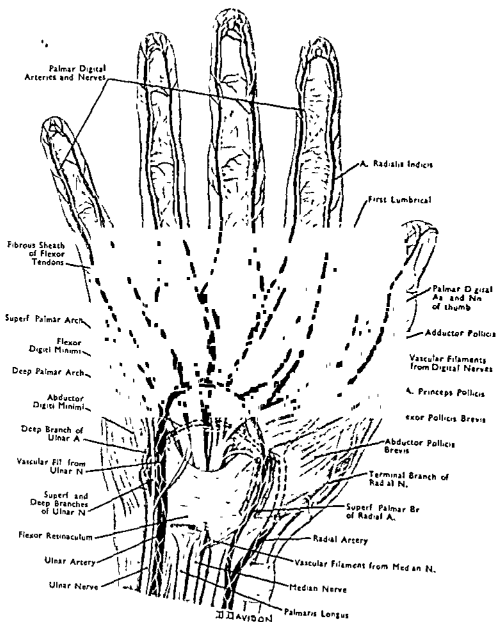


Fig. 34
The palmar arches and digital arteries and their chief vascular nerve supplies

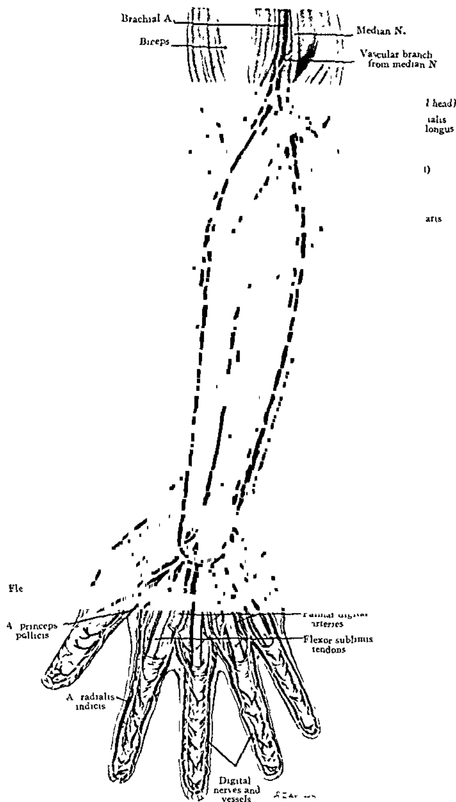


FIG 33
Radial, ulnar and palmar arteries, with their nerve supplies

THE THORACIC PARTS OF THE SYMPATHETIC TRUNKS

The ganglia in this region show an evident segmental arrangement, although twelve ganglia are seldom present (Fig. 35). More often there are ten or eleven ganglia, because the first thoracic is usually fused with the inferior cervical to form a stellate ganglion, and occasionally the last thoracic ganglion is united with the first lumbar ganglion. It is uncommon to find less than ten. Sometimes nodules exist on the interganglionic portions of the trunk or several adjacent ganglia may be partially fused, but intermediate ganglia in the rami communicantes are rare in this region. The ganglia are flattened and triangular, with the apices directed outwards, and they are more uniform in size than those in the cervical region. The lowest ganglia are smaller and somewhat fusiform, and their interganglionic cords are slender and placed obliquely and may easily be mistaken for rami communicantes. The cords between the ganglia are generally single, with occasional duplication or triplication between adjoining ganglia.

The thoracic sympathetic trunks lie in front of the heads of the ribs and the dorsal ends of the intercostal spaces, immediately behind the costal pleura in the endothoracic fascia, but the lower parts incline forwards on the sides of the vertebral bodies as each trunk disappears beneath the medial arcuate (medial lumbocostal) ligament, a tendinous arch in the fascia over the upper part of psoas major, to become continuous with the lumber portion of the sympathetic trunk. Less often the trunk passes between the medial arcuate ligament and the lateral margin of the diaphragmatic crus, or enters the abdomen by piercing the crus alongside the middle thoracic (lesser) splanchnic nerve. The superior intercostal arteries, which supply the first two spaces on each side, run downwards on the lateral sides of the upper parts of the trunks The aortic intercostal arteries, the intercostal veins, and the intercostal nerves run behind them, but occasionally an artery or vein may pass in front On the right side the azygos vein is anteromedial to the trunk and is separated from it by a distinct interval, and on the left side the superior and inferior hemiazygos veins occupy similar relative positions. The descending thoracic aorta, the oesophagus, and the thoracic duct are further forward in the midline and are not in direct relationship to the trunks, although the lower parts of their splanchnic branches are in close proximity to the thoracic duct on the right side and to the descending aorta on the left side.

Direct interconnections between the right and left trunks have not been observed in the thoracic region, but communications between the two could readily be effected through the tenuous retropleural nerve networks which are formed by almost microscopic offshoots from all the adjoining somatic and autonomic nerves (Braeucker,[69] Mitchell[24]).

The thoracic trunks supply or receive the usual communicating, visceral, vascular, muscular, osseous and articular branches. All of these contain a variable proportion of vasomotor fibres, but as most of them are concerned

The palmar arches and digital arteries (Figs. 33, 34).—These are partly innervated by prolongations from the plexuses on the radial and ulnar arteries. In addition the deep arch plexus is reinforced by one or two delicate twigs from the deep branch of the ulnar nerve, and perhaps by radial nerve filaments which accompany the terminal part of the radial artery. The superficial arch receives several accessions of nerve fibres from the medial terminal palmar division of the median nerve and from the superficial terminal or palmar cutaneous branches of the ulnar nerve.

For reasons already given (p. 20) the palmar and digital arteries possess a relatively rich innervation. The digital vessels are surrounded by prolongations from the plexuses on the parent vessels, but they are always reinforced by twigs from the digital nerves. As a rule the little finger and the ulnar half of the ring finger are supplied by the ulnar nerve and the rest of the digits, including the thumb, are innervated on their palmar aspects by the median nerve and on most of their dorsal aspects by the radial nerve.

The veins of the upper limb.—Microscopic examination reveals relatively few nerve fibres in the walls of the veins, and the nerve filaments supplying them are difficult to distinguish. They come from the plexuses around adjacent arteries, or from nearby nerves, e.g the median nerve sometimes supplies a delicate twig to the distal part of the axillary vein.

INNERVATION OF PARIETAL VESSELS

The parietal vessels of the thorax and abdomen are the posterior intercostal, subcostal and lumbar branches of the aorta, the internal mammary arteries (p. 62) with their anterior intercostal, musculophrenic and superior epigastric branches, the suprascapular branches of the thyrocervical trunks (p. 62), the superior intercostal branches of the costocervical trunks (p. 62), the inferior epigastric and deep circumflex iliac branches of the external iliac arteries (p. 78), the iliolumbar branches of the internal iliac arteries (p. 78), and the superficial epigastric, superficial circumflex iliac and superficial external pudendal branches of the femoral arteries (p 78) All these vessels are accompanied and supplied by nerve filaments from the plexuses surrounding the parent vessels and are also joined by small bundles of fibres from adjoining nerves.

The pre-ganglionic fibres for this extensive area of body wall emerge through all the thoracic and the upper lumbar ventral spinal nerve roots and pass to the corresponding thoracic and lumbar sympathetic trunk ganglia in white rami communicantes. After relaying in these ganglia they return in grey rami communicantes to the spinal nerves and are distributed with them to the vascular, glandular, muscular, osseous, articular and other structures in their territories of distribution. The thoracic parts of the sympathetic trunks contain many other important efferent and afferent sympathetic fibres and as they are often the objects of surgical attention they merit description.

: entirely with the innervation of the aorta ...
msidered here.

mmunicating branches.—The thoracic ganglia receive white rami from ıbute grey rami to the adjacent spinal nerves, and in this region some : mixed type. One to four rami are attached to each ganglion and they ıecessarily all pass to the nearest thoracic nerve, as communications : nerves above or below are fairly common. When only one ı attached to a ganglion it is of the mixed type. The grey and ami convey post-ganglionic fibres to the intercostal nerves, which ımongst other structures, the *intercostal vessels.* The proximal parts *osterior intercostal* arteries receive filaments directly from the aortic ınd from the sympathetic trunks or their thoracic splanchnic branches. ıe distal parts receive minute contributions from the intercostal nerves, ılso help to supply the *internal mammary* arteries and their *anterior ıtal, superior epigastric* and *musculophrenic* branches.

ıscular, osseous and articular branches.—These were described in terms on page 53.

INNERVATION OF VESSELS OF LOWER LIMBS

ıe pre-ganglionic fibres for vessels in the lower limbs emerge from the o or three thoracic and first two lumbar segments of the cord and he corresponding parts of the sympathetic trunks in white rami com- ıntes. They relay in the lumbar and upper two or three sacral ganglia returning in grey rami communicantes to adjoining spinal nerves with they are distributed. Some of the post-ganglionic fibres, however, pass y to the iliac arteries, which supply the lower limbs and structures the lower abdomen and pelvis. As the fibres concerned pass through mbar and sacral parts of the sympathetic trunks, and as these are of surgical interest, they will be described before the innervation of the dual vessels is considered.

ıE LUMBAR AND PELVIC PARTS OF THE SYMPATHETIC TRUNKS

These are directly continuous above and below with the thoracic and l portions of the sympathetic trunks respectively, and they lie in the peritoneal tissue behind the peritoneum, on the anterolateral aspects of ertebral column, along the medial margins of the psoas major muscles 36). Rarely they are overlapped by the edges of these muscles. The ar vessels are usually behind them, although on occasion a lumbar y or vein is found in front, and the renal and spermatic vessels are ıor. The right trunk is alongside or partly overlapped by the inferior cava, and the left is just lateral to the abdominal aorta. Both trunks are ntact with the lymph vessels and nodes around the great vessels. The ır part of the right lumbar trunk is close to the cisterna chyli and the

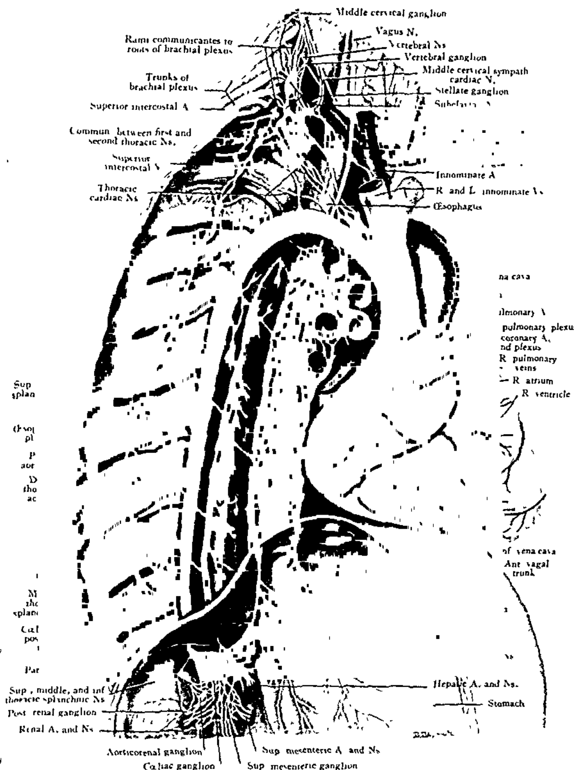


FIG 35

Semi-oblique view of root of neck, thorax and upper abdomen showing the sympathetic ganglionated trunks and their branches, the right vagus nerve, the vagal trunks, the posterior pulmonary, oesophageal and coeliac plexuses, etc.

origin of the thoracic duct At their lower ends they pass downwards behind the common iliac vessels to become the sacral parts of the sympathetic trunks.

Most commonly there are four lumbar ganglia, five or more are exceptional, and only three or even two are sometimes distinguishable. Asymmetry between the two sides is so frequent that it must be regarded as normal. Usually the ganglia are unequal in size and elongated or irregularly flattened in shape. They are inconstant in their positions, and their particular number in the series is determined by their communications with the spinal nerves rather than by their relationship to individual vertebrae. The intervening cords are thicker than those in the thoracic and sacral regions and duplication or triplication is quite common, particularly between the last two lumbar ganglia or between the last lumbar and first sacral ganglia.

The lumbar and sacral portions of the sympathetic trunks are directly continuous with one another behind the common iliac vessels at the level of the pelvic brim Below, the trunks converge and end in front of the coccyx in a single small ganglion, the *caudal ganglion impar* (Fig. 37), or they may be interconnected merely by filaments with no gangliform enlargement. They lie in the retroperitoneal tissue and in the pelvic fascia behind the rectum, just medial to the anterior sacral foramina and the nerves and vessels passing through these apertures Slender transverse or oblique strands interconnect them across the front of the sacrum. The *median sacral vessels* run between them, and small vessels and lymph nodes lie in contact with them; filaments from the trunks supply these structures.

There are rarely five sacral ganglia and the coccygeal or unpaired ganglion is inconstant. More often four sacral ganglia can be distinguished and occasionally only three They are all smaller than the lumbar ganglia and decrease in size from above downwards, the lowest being little larger than a pin's head They are fusiform or triangular in shape and the inter-ganglionic cords are seldom duplicated, except where they become interconnected in front of the coccyx and here three or four filaments are not uncommon.

These lumbar and sacral ganglia supply or receive the usual communicating, visceral, vascular, muscular, osseous and articular branches. Although all contain a varying proportion of vasomotor fibres, many of them are concerned in the innervation of the aorta and visceral arteries and these are not described here.

Communicating branches.—Only the upper two or occasionally three lumbar spinal nerves contribute white rami communicantes to the adjacent lumbar ganglia, but every lumbar spinal nerve receives one or more grey rami communicantes from adjacent lumbar ganglia. Intermediate ganglia are common in the lumbar rami communicantes or in the lumbar ventral nerve roots (p 14) Direct interconnections between the trunks are rare, but are occasionally found in the lower lumbar region: when present they supply one or two filaments to the *median sacral artery.*

Each sacral ganglion supplies one or more grey rami communicantes to

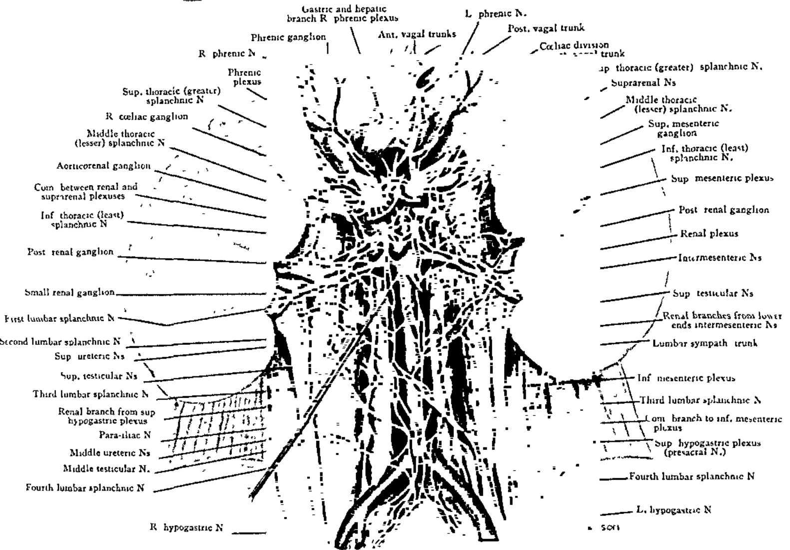


FIG. 36
Autonomic nerves and plexuses in abdomen, showing the lumbar portions of the sympathetic trunks, the lumbar splanchnic nerves, and the coeliac, intermesenteric and superior hypogastric plexuses, etc

or three thoracic and upper two lumbar spinal nerves, and a small proportion may emerge through the roots immediately above or below these segmental levels. Reaching the sympathetic trunks through white or mixed rami communicantes they descend for variable distances before relaying in the lumbar and upper sacral ganglia. Those for the external iliac and femoral arteries relay chiefly in lumbar ganglia, but those for the internal iliac and popliteal arteries and their branches are believed to relay in the upper sacral ganglia. The post-ganglionic vascular fibres resulting from relays in the lumbar ganglia run through grey rami communicantes to the roots of the lumbar plexus and are distributed mainly in the femoral, obturator and genitofemoral branches of this plexus, whereas those resulting from relays in sacral ganglia pass through grey rami chiefly to the first sacral nerves and are distributed mainly in the sciatic nerve and its lateral, and particularly its medial, popliteal divisions.

Post-ganglionic fibres may be carried directly to the internal iliac artery *through inconstant filaments* from adjacent sacral ganglia, but the majority reach it indirectly through branches of the inferior hypogastric plexus and hypogastric nerve or through branches of the sacral plexus. Other vascular *post-ganglionic* fibres are conveyed to the popliteal artery and to the vessels *in the leg* and foot through the sciatic and popliteal nerves.

The common iliac arteries (Fig. 37).—These vessels receive twigs from the [illegible] nchnic nerves, [illegible] the last lumbar or first sacral sympathetic trunk ganglia. *Filaments from the middle* gonadic or ureteric nerves *frequently end in the* periarterial plexus near the end of the common iliac or the beginning *of the* external iliac artery, and a direct supply from the superior hypogastric plexus is sometimes found (Mitchell[202, 242, 243]). *The vascular* filaments from these different sources can generally be traced for *variable distances* along the external and internal subdivisions of the common *iliac arteries*, and occasionally they can be followed as far as the femoral artery.

Mitchell[202] *described* a nerve arising from the lower part of the renal plexus and the second and *third lumbar* splanchnic nerves which descended lateral to the abdominal aorta, communicated with the middle testicular and ureteric nerves, and finally *joined a* filament arising from the superior hypogastric plexus which *ran downwards behind* the common and external *iliac* arteries. In three *female* specimens these post-arterial filaments from *the* superior hypogastric plexuses communicated with the middle ovarian *nerves*, supplied twigs to the *psoas major* muscles and *iliac* arteries, and could be *traced alongside* the common and external iliac *vessels to the* upper thigh. In several subsequent dissections such filaments were *traced to the* femoral arterial bifurcation, but owing to the perivascular network formation it could not be proved that *any of their* fibres were *directly continuous* with those in the lumbar splanchnic nerves or renal plexus. Lazorthes[illegible] *stated* that in a

the adjacent sacral and coccygeal nerves. Their fibres enter the branches of the sacrococcygeal plexus and are distributed with them to the vessels, sweat glands, arrectores pilorum, voluntary muscles, bones and joints in their areas of distribution.

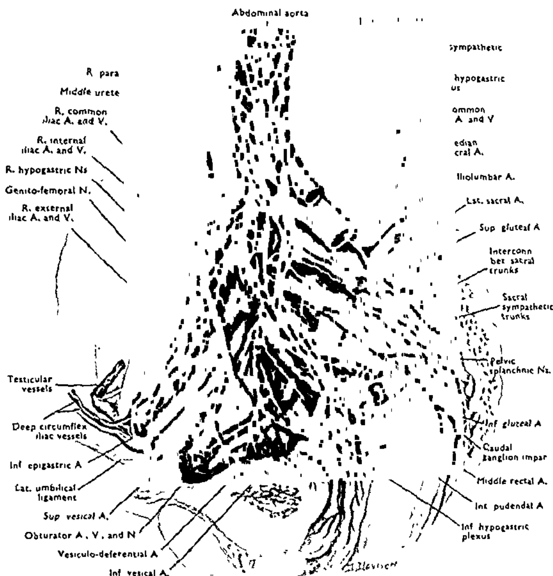


FIG. 37
The chief vascular and nerve structures in the male pelvis.

Apart from the terminal communication(s) in front of the coccyx, the sacral trunks are connected by several transverse or oblique filaments at higher levels.

Vascular branches.—The pre-ganglionic fibres for structures in the pelvis and lower extremities emerge through the ventral nerve roots of the lower two

the groove between the aorta and the Psoas major on a plane superficial to the left sympathetic trunk and its lumbar splanchnic branches. When aberrant renal arteries are present these nerves lie behind them. Just proximal to the level of the aortic bifurcation the para-iliac nerves divide into two to three branches which form a coarse plexus around the corresponding common iliac artery. The fibres are predominantly unmyelinated.

It is interesting to recall that Wrisberg and Valentin both described a remote or distant root of the pelvic or *inferior hypogastric plexus* attached above to the terminal filaments of the superior thoracic (greater) splanchnic nerve and to the renal plexus. This nervelet passed down behind the renal pedicle lateral to the aorta and crossed the pelvic brim to end in the pelvic plexus. Neither Wrisberg nor Valentin mentioned a supply to the iliac arteries, and Wilde traced no branches of the para-iliac nerves to the pelvic plexus. However, there is a general resemblance between these nerves described by Wrisberg, Valentin, Mitchell, Lazorthes and Wilde, and it is possible that they are all variants of the same nerve.

The internal iliac arteries (Fig. 37).—Nerve filaments are continued from the common iliac artery on to the internal iliac artery, and the latter may also receive additional direct contributions from the last lumbar splanchnic nerve, the superior hypogastric plexus (presacral nerve), the homolateral hypogastric nerve, or the first sacral ganglion, but only from one or two and never from all of these sources in the same subject. Direct filaments have not been traced to this artery or its branches from the pelvic splanchnic nerves, but fibres from these nerves reach them through the hypogastric (pelvic) plexuses. Offshoots from the vascular filaments on the internal iliac artery follow all its branches—*superior and inferior vesical, middle rectal, obturator, internal pudendal, superior and inferior gluteal, iliolumbar* and *lateral sacral;* in the female it also supplies *uterine* and *vaginal* branches. As the vessels proceed to their terminations these nervous offshoots are augmented by contributions from the inferior hypogastric plexuses, the hypogastric nerves, or from adjacent branches of the sacrococcygeal plexuses. Some of the fibres help to innervate the vessels and other pass alongside them to the viscera. The latter do not form close perivascular networks, but often lie slightly apart from the vessels.

The **internal pudendal artery** obtains filaments from the first or second sacral ganglia and the inferior hypogastric plexus, and additional bundles from the pudendal nerve which carries many post-ganglionic fibres.

The **obturator artery** receives twigs from the inferior hypogastric plexus and from the obturator nerve. Autonomic afferent and efferent fibres may reach the hip joint along the *acetabular* branch of this artery.

The **superior and inferior gluteal arteries.** Within the pelvis these arteries, along with the internal pudendal, receive filaments from the first or second sacral ganglia, often by a slender common trunk (Lazorthes). In the buttock the gluteal arteries receive additional filaments from the corresponding gluteal

few subjects a filament arising from the second lumbar ganglion passed downwards along the flank of the aorta to reach the posterior surface of the common iliac artery. Wilde[24] described a somewhat similar filament which he termed the *para-iliac nerve* (Figs. 36, 37, 38) and he found that it might arise

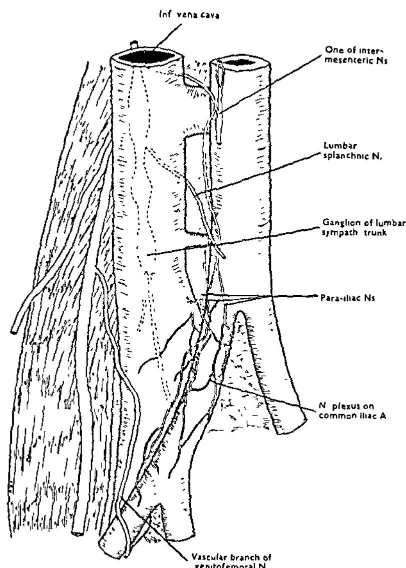


FIG. 38

Outline drawing of a dissection showing the right para-iliac nerve

(*By courtesy of Mr F B Wilde, Manchester University and the Editor and Publishers of the Brit J Surg*)

from the following sources: (1) second and third lumbar splanchnic nerves; (2) *intermesenteric nerves;* (3) *aorticorenal ganglion;* and (4) from a ganglion related to an aberrant renal artery. The para-iliac nerves are bilateral structures and are usually single, but in a few specimens Wilde found two para-iliac nerves on each side The right nerve is situated deeply between the abdominal aorta and the inferior vena cava, and the left nerve lies in

the groove between the aorta and the Psoas major on a plane superficial to the left *sympathetic* trunk and its lumbar splanchnic branches. When aberrant renal arteries are present these nerves lie behind them. Just proximal to the level of the aortic bifurcation the para-iliac nerves divide into two to three branches which form a coarse plexus around the corresponding common iliac artery. The fibres are predominantly unmyelinated.

It is interesting to recall that Wrisberg[illegible] and Valentin[illegible] both described a remote or distant root of the pelvic or inferior hypogastric plexus attached above to the terminal filaments of the superior thoracic (greater) splanchnic nerve and to the renal *plexus* This nervelet passed down behind the renal pedicle lateral to the aorta and crossed the pelvic brim to end in the pelvic plexus. Neither Wrisberg nor Valentin mentioned a supply *to the iliac arteries*, and Wilde traced no branches of the para-iliac nerves to the pelvic plexus. However, there is a general resemblance between these nerves described by Wrisberg, Valentin, Mitchell, Lazorthes and Wilde, *and it is possible that* they are all variants of the same nerve.

The internal iliac arteries (Fig 37).—Nerve filaments are continued from the common iliac artery on to *the internal iliac* artery, and the latter may also receive additional direct contributions from the last lumbar splanchnic nerve, the superior hypogastric plexus (presacral nerve), the homo*lateral hypogastric nerve, or the* first sacral ganglion, but *only* from one or two and never from all of these sources in the same subject. Direct filaments have not been traced to this artery or its branches from the pelvic splanchnic *nerves*, but fibres from these nerves reach them through *the hypogastric* (pelvic) plexuses Offshoots from the vascular filaments on the internal iliac artery follow all its branches—*superior and inferior vesical, middle rectal, obturator, internal pudendal, superior and inferior gluteal, iliolumbar* and *lateral sacral;* in the female it also supplies *uterine* and *vaginal* branches. As the vessels *proceed to their terminations* these nervous offshoots are augmented by contributions from the inferior hypogastric plexuses, the hypogastric nerves, or from adjacent branches of the sacrococcygeal plexuses. Some of the fibres help to innervate the vessels and other pass alongside them to the viscera. The latter do not form close perivascular networks, but often lie slightly apart *from* the vessels

The internal pudendal artery obtains filaments from the first or second sacral ganglia and the inferior *hypogastric plexus*, and additional bundles from the pudendal *nerve which carries many* post-ganglionic fibres.

The obturator artery receives twigs from the inferior hypogastric plexus and from the obturator nerve. Autonomic afferent and efferent fibres may reach the hip joint along the *acetabular* branch of this artery.

The superior and inferior gluteal arteries. Within the pelvis these arteries, along with the internal pudendal, receive filaments from the first or second sacral ganglia, often by a slender common trunk (Lazorthes[illegible]). *In the* buttock the gluteal arteries receive additional filaments from the corresponding gluteal

few subjects a filament arising from the second lumbar ganglion passed downwards along the flank of the aorta to reach the posterior surface of the common iliac artery. Wilde[244] described a somewhat similar filament which he termed the *para-iliac nerve* (Figs. 36, 37, 38) and he found that it might arise

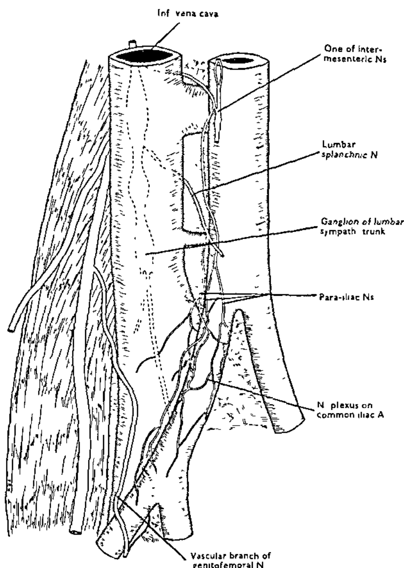


FIG 38

Outline drawing of a dissection showing the right para-iliac nerve

(By courtesy of Mr F R Wilde, Manchester University and the Editor and Publishers of the Brit J Surg)

from the following sources: (1) second and third lumbar splanchnic nerves; (2) intermesenteric nerves; (3) aorticorenal ganglion; and (4) from a ganglion related to an aberrant renal artery. The para-iliac nerves are bilateral structures and are usually single, but in a few specimens Wilde found two para-iliac nerves on each side. The right nerve is situated deeply between the abdominal aorta and the inferior vena cava, and the left nerve lies in

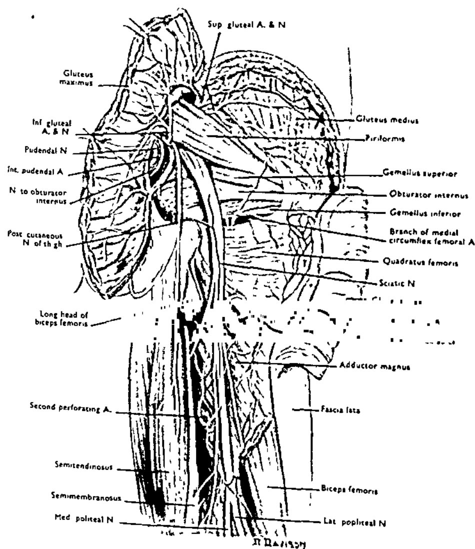


FIG. 39
The gluteal arteries and their main vascular nerve supplies

nerves. Another possible autonomic pathway to the hip joint is via the perivascular nerves of the inferior gluteal artery. Its anastomotic branch unites with others from the circumflex femoral and first perforating arteries to form the *cruciate anastomosis* from which vascular twigs pass to the hip joint: these articular vascula are accompanied by delicate bundles of nerve fibres.

The **iliolumbar and lateral sacral arteries** are supplied mainly by offshoots from the plexus on the parent internal iliac artery, but these may be reinforced by a filament from the first sacral ganglion.

Adjacent structures, such as the sacrum and its ligaments, may be supplied directly from the sacral sympathetic trunks, but more often the post-ganglionic fibres are conveyed through perivascular filaments, *e.g.* the osseous and articular bundles accompanying the various nutrient and articular arteries, or through the numerous nerves derived from the sacrococcygeal plexus. The post-ganglionic fibres reach this plexus through grey rami communicantes. The autonomic fibres for the cutaneous, vascular, glandular and muscular structures travel through similar perivascular and mixed spinal nerve pathways.

The external iliac arteries (Fig 37).—Nerve filaments are continued from the common iliac on to the external iliac artery, and the latter always receives two to four additional twigs from the genitofemoral nerve (Cruveilhier[245]) and its genital branch, which both contain a considerable number of unmyelinated or finely myelinated fibres. This double supply indicates a transition from the visceral to the parietal type of innervation (Delmas and Laux[249]). The highest genitofemoral branch joins the artery near its origin and the lowest near the inguinal ligament, and some of the fibres in the latter are almost certainly prolonged on to the femoral artery, and also along the **inferior epigastric** and **deep circumflex iliac** arteries which derive subsidiary plexuses from that surrounding the parent external iliac artery.

The middle testicular (or ovarian) and ureteric nerves frequently supply a filament or filaments which reach the termination of the common iliac artery or the commencement of the external iliac artery. In a number of subjects it has been possible to trace filaments alongside the external iliac and femoral arteries as far as the point where the profunda femoris arises (p. 75). However, the majority of the external iliac filaments become attenuated as they approach the inguinal ligament, and the femoral perivascular plexus is largely formed by an accession of branches from the femoral nerve. Pacinian corpuscles were not detected either around the common or external iliac arteries (Wilde[187]).

The femoral arteries (Fig. 39).—A few nerve strands from the external iliac plexus pass on to the proximal part of the femoral artery, but the latter artery and its branches (*superficial and deep external pudendal, superficial epigastric, superficial circumflex iliac, arteria profunda femoris, muscular, nutrient, perforating,* and *descending genicular*) receive their main supply from the femoral nerve and its muscular, cutaneous and saphenous branches

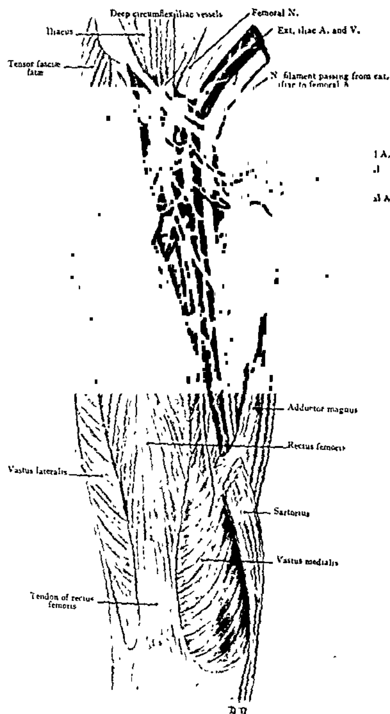


Fig. 40
The femoral artery *with its* main branches and vascular nerves.

(Bichat,[26] Schwalbe,[246] Potts[247]). A comparatively large bundle of fibres from the posterior division of the femoral nerve passes to the point where the artery gives off its profunda branch, and filaments from this bundle supply the main vessel, its deep branch, and the femoral vein; some of these loop around the arterial bifurcation and pursue a recurrent course on the femoral artery and vein as far as the inguinal ligament (Wilde[187]). In the subsartorial (Hunter's) canal reinforcing nervelets are supplied to the main artery by the saphenous nerve and the nerve Vastus medialis. Many Pacinian corpuscles (Fig. 20) and other sensory endings are present in or around the adventitia in the region of the bifurcation, suggesting that it may be a special reflexogenous zone, although Woollard and Weddell[101] could not confirm this experimentally.

According to Hovelacque[221] the femoral artery may also receive a supply from the lateral femoral cutaneous nerve, and Lazorthes[56] claimed that a branch from the anterior division of the obturator nerves reaches the terminal part of the artery or the proximal part of the popliteal artery. Actually when the anterior branch of the obturator nerve emerges from beneath the lower border of Adductor longus it enters the subsartorial canal and often communicates with the saphenous and medial cutaneous branches of the femoral nerve to form the so-called subsartorial plexus, which contributes fine twigs to the femoral artery: usually it is the terminal part of the posterior division of the obturator nerve, and not the corresponding part of the anterior division, which supplies the popliteal artery

Lazorthes[56] stated that the **profunda femoris artery** has a rich innervation and that running along its entire length there is a long vascular branch derived from the posterior division of the femoral nerve; this vascular nerve gives offshoots to the various circumflex, perforating, muscular, and nutrient branches of the artery. The circumflex branches take part in the formation of the **cruciate anastomosis** which supplies vessels to the hip joint, and so both afferent and efferent autonomic fibres could reach the joint along the vascular nerve pathway Wilde[187] has shown that the **circumflex arteries** receive filaments from the nerve to Pectineus, the medial cutaneous nerve of the thigh, and the saphenous nerve. Kiaer[198] reported that pain afferents from the head and neck of the femur in man probably run through sympathetic nerves and the first and second lumbar ganglia; and Freeman *et al.*[200] provided evidence that afferent fibres from the femoral vein in dogs also pass through sympathetic channels (p 39).

The popliteal artery (Fig. 40)—The proximal part is supplied by filaments from the posterior division of the obturator nerve and its articular branch to the knee joint, and from the saphenous branch of the femoral nerve. The remainder of the artery and most of its branches are supplied by filaments from the medial popliteal nerve and its articular branches, but the lateral genicular branches receive additional filaments from the lateral popliteal nerve: the lateral superior genicular artery occasionally receives a direct filament from the termination of the sciatic nerve. The *genicular arteries,*

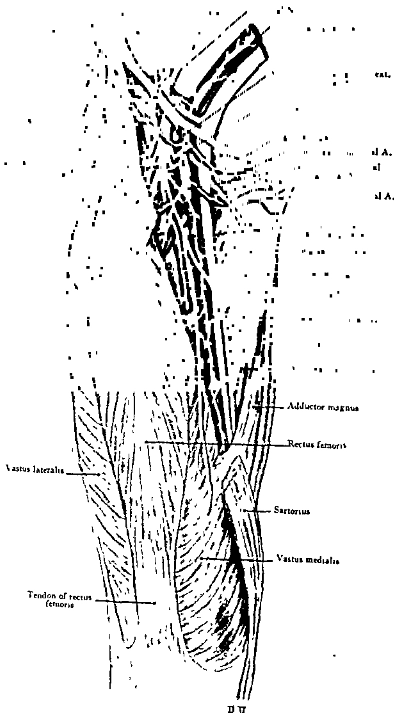


FIG. 40
The femoral artery with its main branches and vascular nerves

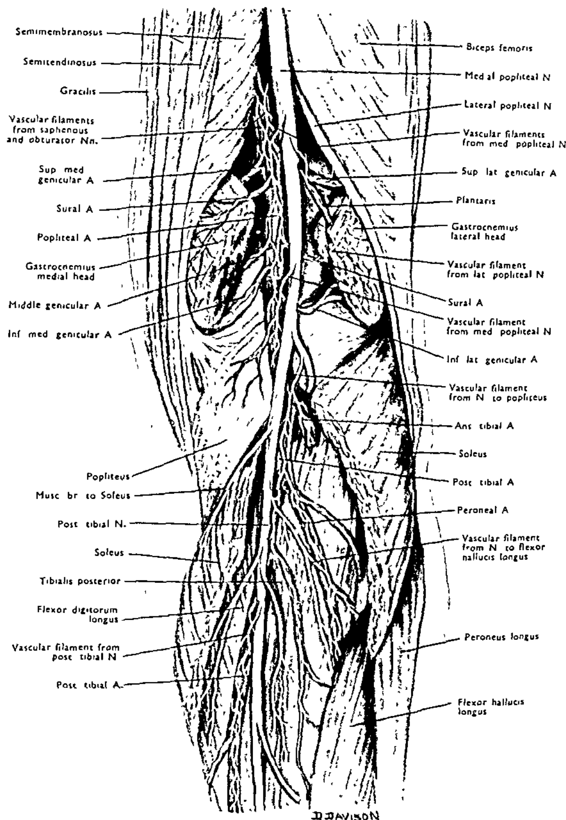


FIG 41
The popliteal artery and the proximal parts of the tibial and peroneal arteries, with their main branches and vascular nerves.

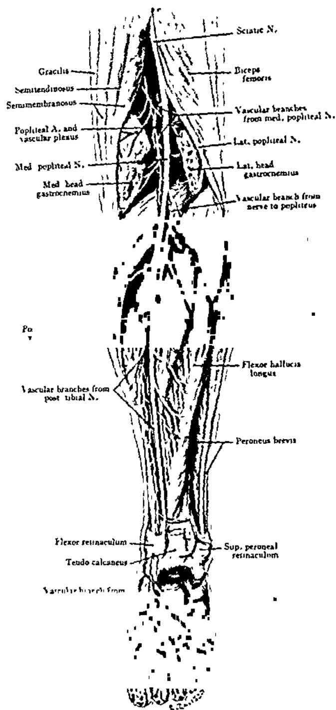


FIG 42
Arteries of popliteal space, dorsal aspect of leg and sole of foot, showing their main vascular nerve filaments

relative to their size, are well innervated and in this feature they resemble other articular vessels. Kellgren and Samuel[248] and Samuel[249] showed that the capsular ligaments of both human and feline knee joints possess a profuse nerve plexus and a variety of specialised and unspecialised nerve endings, most of which are somatic. They also demonstrated a more delicate nerve network in the synovial membrane and around its vessels, mostly composed of sympathetic fibres.

The tibial arteries (Figs. 41, 42).—The tibial arteries and their branches are supplied by filaments from the tibial nerves and their branches, which are the continuations of the medial and lateral popliteal divisions of the sciatic nerve.

The **posterior tibial artery** receives filaments from the nerve to Popliteus and lower down it is supplied by twigs from the posterior tibial nerve or its muscular branches to Tibialis posterior, Flexor digitorum longus, or Flexor hallucis longus. The proximal and distal parts of the artery are more richly innervated than the intervening portion. The reinforcing filaments to the distal part come from the termination of the posterior tibial nerve or from the commencement of its medial or lateral plantar branches, and they are often associated with articular branches to the ankle joint. According to Lazorthes[56] all these filaments form a well-defined plexus on the last 8 - 10 cm of the artery which he terms the retromalleolar posterior tibial plexus

Subsidiary plexuses are prolonged around its *circumflex fibular, peroneal, nutrient, muscular, malleolar, communicating, calcanean* and *plantar* branches

The **peroneal artery** may receive a twig from the nerve to Popliteus (Potts[247]), and this may be associated with the filament supplying the posterior tibial artery. The peroneal artery also receives additional filaments from the posterior tibial nerve or its branches to Flexor hallucis longus, Tibialis posterior or Soleus Delicate bundles of nerve fibres are continued along the *nutrient, muscular, perforating, communicating* and *calcanean* branches of this artery.

The **anterior tibial artery.**—The proximal part, situated on the back of the leg before it passes forwards between the two heads of Tibialis posterior, is innervated by a twig from the nerve to Popliteus, and this vascular filament may be associated with a tiny nerve supplying the superior tibiofibular joint (Hovelacque[221]). The main part of the vessel on the front of the leg is innervated by three to five delicate branches from the anterior tibial nerve or from its offshoots supplying Tibialis anterior. The terminal part of the artery may receive twigs from the articular branch to the ankle joint supplied by the anterior tibial nerve Its branches (*tibial recurrent, muscular* and *malleolar*) are accompanied by filaments from the plexus around the parent vessel, but they may receive direct supplementary twigs from adjacent nerves; for example the posterior tibial recurrent artery may get a filament from the nerve to Popliteus and the lateral malleolar artery may be supplied by a delicate bundle from the lateral terminal branch of the anterior tibial nerve

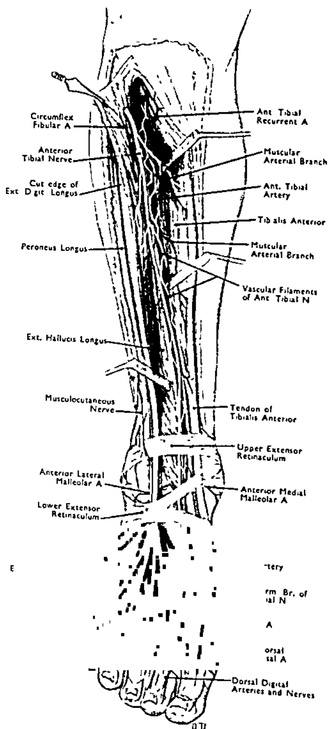


FIG. 43
The anterior tibial artery and the arteries on the dorsum of the foot, with their chief vascular nerve filaments.

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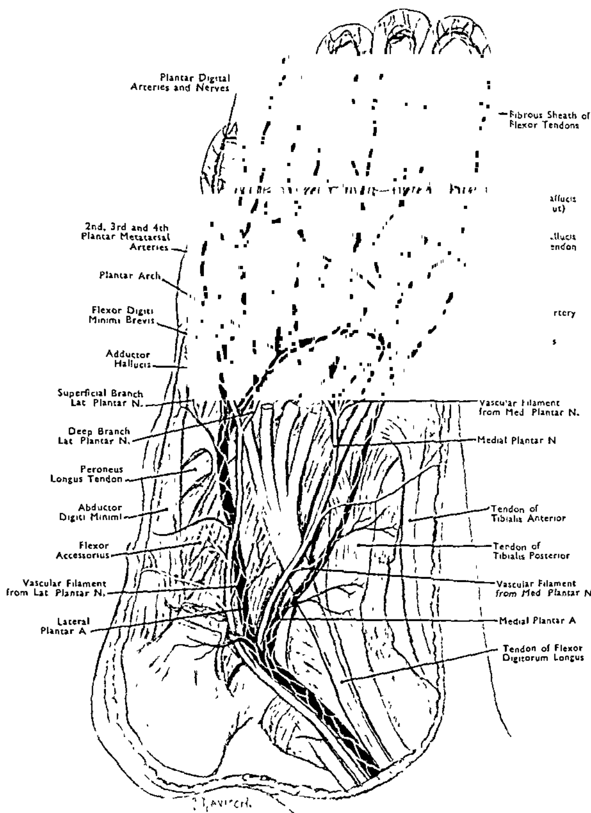


FIG. 44
The plantar arteries with their main branches and vascular nerve filaments

The **arteria dorsalis pedis** (Fig. 42) is the continuation of the anterior tibial artery and it is supplied by the anterior tibial nerve and its medial terminal branch. Its branches are the *tarsal, arcuate, dorsal metatarsal* and [illegible] minute bundles of fibres go with them from the plexus [illegible] or sural nerves.

The plantar arteries (Figs. 41, 43).—The plantar arteries are innervated in their proximal parts by continuations of nerve filaments from the rich plexus around the termination of the posterior tibial artery. The more distal portions of both the medial and lateral vessels receive extra filaments from the corresponding medial and lateral plantar nerves. Like the palmar arches, their innervation is comparatively abundant, and this is true also of their plantar metatarsal and digital branches. The plantar *digital* arteries receive delicate contributions from the adjacent plantar digital nerves, those for the inner three and a half digits coming from the medial plantar nerve and the remainder from the lateral plantar nerve.

The veins of the lower limbs.—The nerve filaments supplying these vessels are minute and difficult to find macroscopically. They are irregular in their origins and come from adjacent periarterial plexuses. Less constantly tiny bundles from nearby nerves are seen entering the adventitia of the larger veins, *e.g.*, filaments joining the femoral vein from the corresponding nerve and the popliteal vein from the medial popliteal nerve.

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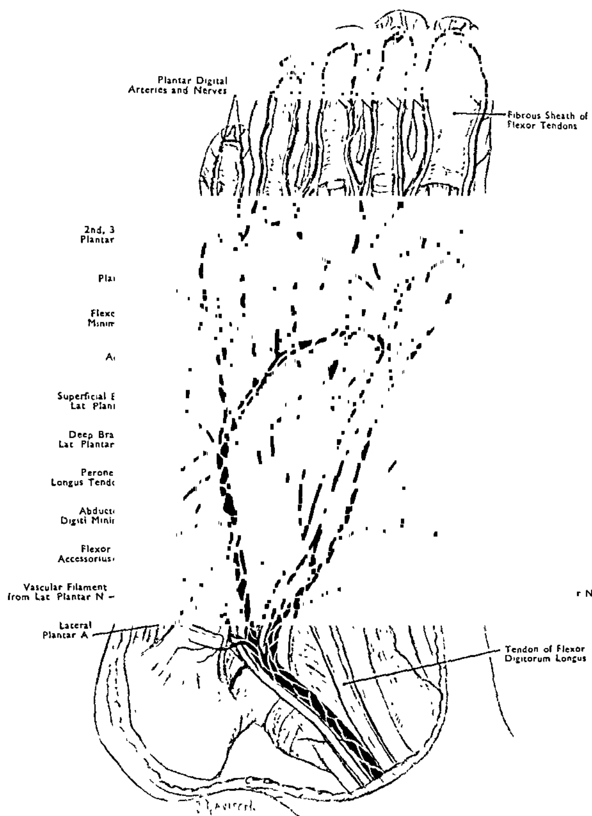


FIG. 44
The plantar arteries with their main branches and vascular nerve filaments

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CHAPTER II

SYNOPSIS OF ANATOMY OF PERIPHERAL ARTERIES*

WITH NOTES ON VARIATIONS AND COLLATERAL CIRCULATIONS

THE ARTERIES OF THE UPPER LIMB

THE main arterial trunk runs through the root of the neck, the axilla and the arm as far as the elbow before bifurcating opposite the neck of the radius into the radial and ulnar arteries. The parts in the neck, axilla and arm are termed respectively the subclavian, axillary and brachial arteries. Besides being the main trunk for the upper limb, each subclavian artery also supplies important branches to structures in the head, neck and thorax, and to the thoracic and upper abdominal parietes.

THE SUBCLAVIAN ARTERIES

The right arises from the innominate artery and the left from the aortic arch, and both curve *outwards behind the corresponding Scalenus anterior.* The parts lying proximal, posterior and distal to this muscle are termed first, second and third respectively.

The first part of the right subclavian artery is about three inches (7.5 cm.) long and begins behind the corresponding sternoclavicular joint. It curves upwards and outwards, rising about four-fifths of an inch (2.0 cm.) above the clavicle, being covered by the Sternomastoid, Sternohyoid and Sternothyroid, the last two muscles separating it from the anterior jugular vein. It is crossed anteriorly from above down by the right vagus nerve, by cardiac branches of the vagus and sympathetic, by the internal jugular and vertebral veins and by the termination of the right lymphatic duct. The ansa subclavia and right recurrent laryngeal nerve loop around it. Lying postero-inferior are the stellate ganglion, the apex of the lung covered by the cervical pleura and the suprapleural membrane, the Longus cervicis, the first thoracic vertebra and occasionally an accessory vertebral vein.

The first part of the left subclavian artery springs from the aortic arch behind the left common carotid about the level of the lower margin of the third thoracic vertebra and opposite the left border of the manubrium sterni. It ascends to the root of the neck before arching laterally to the medial border of Scalenus anterior.

* Illustrations of the *arteries and their main branches appear in Chapter I on* "The Innervation of Peripheral Blood Vessels"

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on one or both sides from the second

The vertebral artery, apart from a few branches to the deep muscles of the neck, supplies structures within the head and spinal canal. It is not included, therefore, amongst peripheral arteries.

The internal mammary artery descends behind the upper six costal cartilages about half-an-inch (1·25 cm.) lateral to the sternum, and divides opposite the xiphi-sternal junction into musculophrenic and superior epigastric branches. It has the usual venae comites, and alongside there are four to five lymph nodes. The lymph afferents for these nodes come from the anterior thoracic wall, from the abdominal wall above the umbilicus, from the medial parts of the mammary gland and from the upper surface of the liver.

It provides two small *anterior intercostal arteries* for each of the upper six intercostal spaces, and these run laterally to anastomose with the posterior intercostal arteries and their collateral branches. *Perforating* branches emerge through the anterior ends of the same intercostal spaces and help to supply the pectoral muscles, the mammary glands, and the skin and subcutaneous tissues over the front of the chest. A few small sternal branches supply the sternum and the Sternocostalis, and the other intrathoracic branches are distributed to the pleura, pericardium, phrenic nerve, Diaphragm, mediastinal connective tissue, lymph nodes and the remains of the thymus.

The superior epigastric artery enters the sheath of the Rectus abdominis by passing through the interval between the xiphoid and costal origins of the Diaphragm. It suppli[illegible]
and twigs pass to th[illegible]
ligament of the liver [illegible]
but there is a fairly constant interconnection in front of the xiphoid process, and the terminal branches anastomose freely with corresponding branches of the inferior epigastric artery.

The musculophrenic artery runs downwards and outwards behind the seventh, eighth and ninth costal cartilages and enters the uppermost part of the abdominal wall by perforating the Diaphragm near the eighth or ninth costal cartilage. It gives off the small *anterior intercostal arteries* for the seventh, eighth and ninth intercostal spaces and supplies twigs to the pericardium, Diaphragm and abdominal muscles. Its terminal branches anastomose with those of the phrenic arteries and with the ascending branch of the deep iliac circumflex artery.

The thyrocervical trunk is short and divides almost immediately under cover of the internal jugular vein into the inferior thyroid, transverse cervical and suprascapular arteries.

The inferior thyroid artery ascends on the antero-medial border of Scalenus anterior and turns medially, at the level of the cricoid cartilage, in front of the vertebral artery and behind the carotid sheath, before descending for a short distance on Longus cervicis to reach and supply the homolateral

In the thorax the left lung and pleura lie lateral to it, and medially are the trachea, one or two lymph nodes, the left recurrent laryngeal nerve, the oesophagus and the thoracic duct. In front are the left common carotid artery, the left innominate vein, the left vagus and some vagal and sympathetic cardiac branches: the left phrenic nerve is antero-lateral. Behind it lies close to the left border of the oesophagus and the thoracic duct.

The cervical portion of the first part of the left subclavian artery corresponds closely in its disposition and relationships to that on the right side. The chief differences are: the left phrenic nerve and the terminal part of the thoracic duct are anterior, while the left recurrent laryngeal nerve does not loop around it but around the aortic arch.

The second parts of the right and left subclavian arteries have almost the same courses and relationships. Each forms the highest part of the arterial arch and corresponds to the short portion of the artery lying behind Scalenus anterior, which separates it from the homolateral subclavian and anterior jugular veins and from the transverse cervical and suprascapular arteries. On the right side the phrenic nerve is separated from the second part of the artery by the Scalenus anterior, but on the left side it crosses the first part of the artery close to the medial border of this muscle The lung, covered by pleura and suprapleural membrane, lies below and behind the second part of the artery; the lower trunk of the brachial plexus and the (inconstant) Scalenus minimus are posterior; and the middle and upper trunks of this plexus are superior. A variable number of inferior deep cervical lymph nodes are related to the artery.

The third parts of the subclavian arteries are the most superficial, being covered only by skin, fascia and Platysma. Each extends from the lateral border of Scalenus anterior, continues across the subclavian portion of the posterior triangle of the neck and then behind the clavicle and the Subclavius to the outer margin of the first rib where it becomes the axillary artery. It is crossed by the small nerve to Subclavius, by the inconstant accessory phrenic nerve and by the suprascapular artery, and it is covered by a venous plexus formed by the suprascapular, transverse cervical and anterior jugular veins draining into the external jugular and subclavian veins The Scalenus medius lies behind the artery, with the lower trunk of the brachial plexus intervening; and above and lateral are the middle and upper trunks and the inferior belly of the Omohyoid At its termination the artery is situated behind the clavicle and Subclavius and rests in the posterior of the two shallow grooves on the upper surface of the first rib

Branches

The branches of the subclavian artery are. (1) vertebral; (2) internal mammary; (3) thyrocervical trunk, and (4) costocervical trunk. On the left side all arise from the first part of the artery, but on the right side the costo-cervical trunk arises from the second part. Occasionally the ascending cervical

or suprascapular arteries arise directly on one or both sides from the second or third parts of the artery.

The vertebral artery, apart from a few branches to the deep muscles of the neck, supplies structures within the head and spinal canal. It is not included, therefore, amongst peripheral arteries.

The internal mammary artery descends behind the upper six costal cartilages about half-an-inch (1 25 cm.) lateral to the sternum, and divides opposite the xiphi-sternal junction into musculophrenic and superior epigastric branches. It has the usual venae comites, and alongside there are four to five lymph nodes. The lymph afferents for these nodes come from the anterior thoracic wall, from the abdominal wall above the umbilicus, from the medial parts of the mammary gland and from the upper surface of the liver.

It provides two small *anterior intercostal arteries* for each of the upper six intercostal spaces, and these run laterally to anastomose with the posterior intercostal arteries and their collateral branches. *Perforating* branches emerge through the anterior ends of the same intercostal spaces and help to supply the pectoral muscles, the mammary glands, and the skin and subcutaneous tissues over the front of the chest. A few small sternal branches supply the sternum and the Sternocostalis, and the other intrathoracic branches are distributed to the pleura, pericardium, phrenic nerve, Diaphragm, mediastinal connective tissue, lymph nodes and the remains of the thymus

The superior epigastric artery enters the sheath of the Rectus abdominis by passing through the interval between the xiphoid and costal origins of the Diaphragm It supplies the upper part of the Rectus and the overlying skin, and twigs pass to the Diaphragm and on the right side into the falciform ligament of the liver. The arteries of the two sides do not communicate freely, but there is a fairly constant interconnection in front of the xiphoid process, and the terminal branches anastomose freely with corresponding branches of the inferior epigastric artery.

The musculophrenic artery runs downwards and outwards behind the seventh, eighth and ninth costal cartilages and enters the uppermost part of the abdominal wall by perforating the Diaphragm near the eighth or ninth costal cartilage It gives off the small *anterior intercostal arteries* for the seventh, eighth and ninth intercostal spaces and supplies twigs to the pericardium, Diaphragm and abdominal muscles Its terminal branches anastomose with those of the phrenic arteries and with the ascending branch of the deep iliac circumflex artery

The thyrocervical trunk is short and divides almost immediately under cover of the internal jugular vein into the inferior thyroid, transverse cervical and suprascapular arteries

The inferior thyroid artery ascends on the antero-medial border of Scalenus anterior and turns medially, at the level of the cricoid cartilage, in front of the vertebral artery and behind the carotid sheath, before descending for a short distance on Longus cervicis to reach and supply the homolateral

lobe of the thyroid gland. The middle cervical ganglion of the sympathetic trunk and the recurrent laryngeal nerve usually lie anterior to this artery, but occasionally both may lie behind it. On the left side the termination of the thoracic duct is another anterior relation.

Besides its thyroid branches, it contributes to the laryngeal, tracheal, pharyngeal and oesophageal blood supply, and provides muscular branches to adjacent muscles, both directly and through its small *ascending cervical* branch which runs upwards in the groove between Longus capitis and Scalenus anterior. This ascending cervical artery gives off small spinal branches, and it anastomoses with branches of the vertebral, ascending pharyngeal, occipital and deep cervical arteries. It is accompanied by a paravascular nerve which occasionally contains tiny groups of ganglion cells.

The transverse cervical artery runs laterally in front of the Scalenus anterior, phrenic nerve and brachial plexus, and deep to the Sternomastoid and internal jugular vein. Crossing the floor of the posterior triangle of the neck it divides opposite the anterior margin of Levator scapulae into superficial and deep branches. The former runs upwards beneath Trapezius, supplying it and neighbouring muscles, and anastomosing with descending twigs from the occipital artery. The latter runs downwards under cover of the Levator scapulae and the Rhomboids, close to the medial border of the scapula, sending offshoots into the muscles of the supraspinous, infraspinous and subscapular fossae which anastomose with branches of the suprascapular and subscapular arteries: it also helps to supply the Trapezius, Latissimus dorsi and Rhomboids, and some of these muscular branches anastomose with posterior branches of the posterior intercostal arteries.

The suprascapular artery begins behind the Sternomastoid and the internal jugular vein. It inclines outwards and downwards across Scalenus anterior, the phrenic nerve, the brachial plexus and the subclavian artery, and continues behind the clavicle, Subclavius and inferior belly of the Omohyoid. Reaching the suprascapular notch on the superior border of the scapula, it passes above (or occasionally below) the suprascapular ligament, which separates it from the suprascapular nerve, before descending through the supraspinous fossa, deep to the Supraspinatus and behind the neck of the scapula. It runs onwards through the spinoglenoid (great scapular) notch, deep to the spinoglenoid ligament and ends beneath Infraspinatus by anastomosing with the circumflex scapular artery and the deep branch of the transverse cervical artery. As it runs over the suprascapular ligament it gives off a branch which enters the subscapular fossa to anastomose with branches of the subscapular and transverse cervical arteries.

It supplies branches to adjacent muscles such as Sternomastoid, Subclavius, Subscapularis, Supraspinatus and Infraspinatus; a *suprasternal* branch that runs over the sternal end of the clavicle to the skin over the upper part of the chest; and an *acromial* branch which pierces Trapezius and ramifies over the acromion process, anastomosing with the acromial branches of the

acromiothoracic and posterior circumflex arteries. The suprascapular artery also sends twigs to the sternoclavicular, acromioclavicular and shoulder joints and nutrient arteries to the clavicle and scapula.

The costocervical trunk arises from the second part of the subclavian artery on the right side and from the first part of the artery on the left side. Arching backwards over the suprapleural membrane and lung apex it reaches the neck of the first rib, where it ends by dividing into superior intercostal and deep cervical branches.

The superior intercostal artery descends behind the pleura, medial to the first thoracic nerve, lateral to the sympathetic trunk and in front of the necks of the first and second ribs. It supplies the *posterior intercostal arteries* of the upper two spaces, and they and their collaterals anastomose with the corresponding anterior intercostal branches of the internal mammary artery. As a rule the second posterior intercostal artery is joined by a branch from the third, and occasionally this communication is so large that the posterior intercostal artery of the second space may be regarded as an aortic rather than as a superior intercostal derivative. Rarely the entire superior intercostal artery is absent, its place being taken by first or second aortic intercostal arteries arising directly from the aorta.

The deep cervical artery is usually a branch of the costocervical trunk, but occasionally it originates directly from the subclavian artery. It is analogous to the posterior branch of a posterior intercostal artery and it passes backwards above the eighth cervical nerve and between the transverse process of the seventh cervical vertebra and the neck of the first rib, or less commonly between the transverse processes of the sixth and seventh cervical vertebrae It then ascends in the back of the neck between the Semispinalis capitis and Semispinalis cervicis as high as the axis, supplying the adjacent muscles, anastomosing with branches of the ascending cervical and vertebral arteries en route, and ending by anastomosing with the deep division of the descending branch of the occipital artery.

VARIATIONS

The right subclavian artery may arise from the innominate above or below the level of the sternoclavicular joint, or it may originate directly from the aortic arch as its first or last branch. When it is the first branch it occupies the same position as the innominate artery, and when it is the last it arises near the termination of the arch and runs obliquely upwards and to the right, behind or between the trachea and the oesophagus, to the root of the neck, whence it pursues its normal course. Rarely the artery passes in front of, or through, the Scalenus anterior, and occasionally the subclavian vein accompanies the artery behind this muscle. Sometimes two innominate arteries exist, so that the left common carotid and subclavian arteries are fused at their origins, and very rarely the three normal branches of the aortic

arch arise by one single stem. All these variants and others exist as the normal arrangement in various lower animals.

The actual branches of the subclavian artery may arise more medial or lateral than usual, and they in themselves show considerable irregularities in their branchings, but the variations in height reached by the artery in the neck are of more practical importance. It may arch up to one-and-a-half inches (4 cm.) above the clavicle, that is about twice the average height, or it may not rise above the level of the upper border of this bone.

Collateral Circulation

Operations on the first part of the subclavian artery are seldom performed and the majority of operations on this vessel have involved its second and third parts. The collateral circulation developing following the latter operations is virtually the same as that for the first part of the axillary artery (p. 101).

If the first part is tied off a collateral circulation is established through dilatation of existing anastomoses such as those between: (1) the vertebral arteries of opposite sides; (2) the superior and inferior thyroids; (3) the deep cervical artery and descending branches of the occipital; (4) the internal mammary and its anterior intercostal branches with the inferior epigastric and aortic intercostal arteries; (5) the superior intercostal and upper aortic intercostal arteries; and (6) the scapular branches of the transverse cervical, suprascapular and subscapular arteries with branches of the intercostal arteries.

THE AXILLARY ARTERY

This is the continuation of the subclavian artery and runs from the outer border of the first rib to the lower border of Teres major where it becomes the brachial artery. It is crossed by the Pectoralis minor and for descriptive purposes the portions of the artery proximal to, behind and distal to this muscle are referred to as the first, second and third parts respectively. The direction of the artery varies with the position of the arm, being convex upwards when the arm is by the side, almost straight when the arm is horizontal, and convex downwards when the arm is raised vertically.

The first part is short and lies deeply beneath Pectoralis major and the clavipectoral fascia, enclosed along with the axillary vein and cords of the brachial plexus in a fibrous sheath prolonged from the prevertebral layer of the deep cervical fascia. The cephalic and acromiothoracic veins pierce the clavipectoral fascia and axillary sheath in front of the artery to end in the axillary vein, and the lateral pectoral nerve and the loop connecting it and the medial pectoral nerve also cross it anteriorly. Behind it are the first intercostal space, the upper digitations of the Serratus anterior, the medial cord of the brachial plexus, the medial pectoral nerve and the nerve to Serratus anterior. The lateral and posterior cords of the brachial plexus and

the lateral pectoral nerve lie laterally, and medially it is overlapped by the axillary vein. The apical axillary lymph nodes are mainly antero-internal to the proximal parts of the axillary vessels and *their efferents* unite to form the subclavian lymphatic trunk

The second part is subjacent to Pectorales major and minor and behind it are the posterior cord of the brachial plexus and Subscapularis. *Medially* are the axillary vein with the medial cord of the plexus intervening, the medial pectoral nerve and some lymph nodes. Laterally are the lateral cord of the plexus and Coracobrachialis.

The third part is covered distally only by skin and fascia, but proximally it is also covered by the lower part of Pectoralis major and it is crossed by the medial root of the median nerve. Behind it rests upon the lower part of Subscapularis, the tendons of the Latissimus dorsi and Teres major, and the circumflex and radial nerves. Laterally are the median and musculocutaneous nerves and the Coracobrachialis. Medially is the axillary vein, separated from the artery by the medial cutaneous nerve of the forearm in front and by the ulnar nerve behind; the medial cutaneous nerve of the arm runs medial to the vein Occasionally the artery is covered by thin vestigial musculo-aponeurotic remnants arching across the floor of the axilla, such as the *Chondro-Epitrochlearis, Dorso-Epitrochlearis,* and *Costo-Coracoideus.*

The axillary vein is the continuation of the basilic vein and it is joined by the brachial venae comites near the lower margin of Subscapularis. The *lateral group of axillary lymph nodes are located mainly postero-medial to* the axillary vessels.

BRANCHES

The superior thoracic artery is a small branch which supplies mainly the adjacent pectoral and intercostal muscles and lymph nodes. It anastomoses with branches of the acromiothoracic, suprascapular, internal mammary and intercostal arteries

The acromiothoracic artery is a short trunk which arises beneath Pectoralis minor and runs around its upper border to pierce the clavipectoral fascia. It then divides beneath Pectoralis major into clavicular, pectoral, acromial and deltoid branches.

The clavicular branch is slender and supplies mainly the Subclavius and the sternoclavicular joint. It anastomoses with branches of the superior thoracic, suprascapular and internal mammary arteries.

The pectoral branch is larger and descends between the two pectoral muscles, distributing twigs to both. It anastomoses with the anterior intercostal and lateral thoracic arteries

The acromial branch pierces the Deltoid and ramifies over the acromion process, uniting with branches from the suprascapular, deltoid and posterior circumflex humeral arteries.

The deltoid or humeral branch runs in the groove between Deltoid and Pectoralis major, beside the cephalic vein, supplying these muscles and the

overlying skin and anastomosing with the acromial branch and with the anterior circumflex humeral artery.

The lateral thoracic artery also arises beneath Pectoralis minor and runs along its lateral border, supplying the adjacent muscles and sending off one or more external mammary branches to the outer part of the mamma. It anastomoses with branches of the internal mammary, intercostal and subscapular arteries.

The subscapular artery, the largest branch, arises about the level of the lower border of Subscapularis and follows it to the inferior angle of the scapula, supplying the adjacent muscles, lymph nodes and parietes. It anastomoses with branches of the lateral thoracic, intercostal and transverse cervical arteries.

Near its origin the subscapular artery gives off the *circumflex scapular artery* which is usually larger than the continuation of the parent vessel. It passes backwards through the *triangular space* bounded by Subscapularis above, Teres major below and the long head of Triceps laterally, and enters the infraspinous fossa by turning around the lateral scapular border. It gives off branches to the muscles mentioned and also to the Teres minor, Deltoid and Infraspinatus Its terminal branches ramify in the infraspinous and subscapular fossae, anastomosing with the terminations of the suprascapular artery and the deep branch of the transverse cervical artery: and the triceps and deltoid branches unite with an ascending branch of the arteria profunda brachii.

The anterior circumflex humeral artery is a slender branch which arises near, or in common with, the posterior circumflex. It runs laterally deep to the Coracobrachialis, Biceps and Deltoid, and forms with the corresponding posterior artery a vascular collar around the surgical neck of the humerus. It supplies the adjacent muscles, the shoulder joint and the head of the humerus.

The posterior circumflex humeral artery is larger than the anterior circumflex artery and accompanies the circumflex nerve backwards through the *quadrangular space* bounded by Subscapularis and Teres minor above, the Teres major below, the long head of Triceps medially and the surgical neck of the humerus laterally. It curves around the posterior part of the surgical neck to anastomose with the termination of the anterior circumflex and with branches of the suprascapular, acromiothoracic and profunda brachii arteries. It helps to supply Deltoid, Triceps, Teres major and Teres minor, the shoulder joint, and the upper end of the humerus.

Variations

Anomalies of the axillary artery, apart from minor variations in the size and arrangement of its branches, are uncommon, although rarely the brachial artery is missing, the radial and ulnar arteries arising directly from the

ax [illegible]

b[illegible] which is then larger than the from the former by a common stem vessel which is then larger than the continuation of the artery and which is surrounded by the chief nerves derived from the brachial plexus. Occasionally the humeral circumflex arteries arise together, or the posterior one may be given off from the profunda brachii artery, and very rarely the common or anterior interosseous arteries of the forearm originate directly from the axillary artery. Inconstant branches are sometimes seen, such as a small alar thoracic vessel which is distributed to the lymph nodes and fat in the apex of the axilla.

Collateral Circulation

After ligature of the distal part of the subclavian artery, or of the proximal part of the axillary above the origin of its acromiothoracic branch, an extensive collateral circulation can be established between branches: (1) of the suprascapular, transverse cervical, acromiothoracic and subscapular arteries; (2) of the internal mammary, superior intercostal, aortic intercostal, lateral thoracic and subscapular arteries; and (3) by the dilatation of previously inconspicuous branchlets of both the subclavian and axillary arteries which may form a tortuous plexus within the axilla.

If the axillary artery is tied between the origins of its acromiothoracic and subscapular branches, the chief collateral channels are those between the transverse cervical, suprascapular and subscapular arteries: but the anastomoses mentioned above between the acromiothoracic and lateral thoracic arteries with the internal mammary, intercostal, humeral circumflex and subscapular arteries also enlarge and assist in maintaining the circulation.

Ligatures applied to the third part of the artery are generally below the subscapular and humeral circumflex arteries, and then the circulation has to be maintained by enlargement of the anastomoses between these arteries and the profunda brachii, including the numerous muscular branches which may become very tortuous and dilated.

THE BRACHIAL ARTERY

This is the direct continuation of the axillary artery and it ends in the cubital fossa by dividing into the *radial and ulnar arteries*. At first medial to the humerus, it inclines gradually forwards, and at the elbow it is midway between the humeral epicondyles. Thus if the artery has to be compressed for any reason pressure must be directed laterally in the upper part of the arm and backwards in the lower part.

It lies in the groove medial to Coracobrachialis and Biceps, covered by the skin and superficial and deep fascia, the latter being reinforced in front of the elbow by the bicipital aponeurosis which intervenes between the artery and the median cubital vein—a relationship of some practical importance.

overlying skin and anastomosing with the acromial branch and with the anterior circumflex humeral artery.

The lateral thoracic artery also arises beneath Pectoralis minor and runs along its lateral border, supplying the adjacent muscles and sending off one or more external mammary branches to the outer part of the mamma. It anastomoses with branches of the internal mammary, intercostal and subscapular arteries.

The subscapular artery, the largest branch, arises about the level of the lower border of Subscapularis and follows it to the inferior angle of the scapula, supplying the adjacent muscles, lymph nodes and parietes. It anastomoses with branches of the lateral thoracic, intercostal and transverse cervical arteries.

Near its origin the subscapular artery gives off the *circumflex scapular artery* which is usually larger than the continuation of the parent vessel. It passes backwards through the *triangular space* bounded by Subscapularis above, Teres major below and the long head of Triceps laterally, and enters the infraspinous fossa by turning around the lateral scapular border. It gives off branches to the muscles mentioned and also to the Teres minor, Deltoid and Infraspinatus. Its terminal branches ramify in the infraspinous and subscapular fossae, anastomosing with the terminations of the suprascapular artery and the deep branch of the transverse cervical artery: and the triceps and deltoid branches unite with an ascending branch of the arteria profunda brachii.

The anterior circumflex humeral artery is a slender branch which arises near, or in common with, the posterior circumflex. It runs laterally deep to the Coracobrachialis, Biceps and Deltoid, and forms with the corresponding posterior artery a vascular collar around the surgical neck of the humerus. It supplies the adjacent muscles, the shoulder joint and the head of the humerus.

The posterior circumflex humeral artery is larger than the anterior circumflex artery and accompanies the circumflex nerve backwards through the *quadrangular space* bounded by Subscapularis and Teres minor above, the Teres major below, the long head of Triceps medially and the surgical neck of the humerus laterally. It curves around the posterior part of the surgical neck to anastomose with the termination of the anterior circumflex and with branches of the suprascapular, acromiothoracic and profunda brachii arteries. It helps to supply Deltoid, Triceps, Teres major and Teres minor, the shoulder joint, and the upper end of the humerus.

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Variations

The brachial artery seldom bifurcates below the level of the cubital fossa, but it often divides at a higher level and the ulnar, radial and interosseous arteries are all involved. Most commonly the radial artery arises high up, even in the axilla, and the other division forms the ulnar and common interosseous arteries. Less commonly this arrangement is reversed, the ulnar artery arising above, and the radial and interosseous arteries by a common stem; or the interosseous vessel may arise high up and the main stem may then divide into radial and ulnar divisions about the customary level opposite the radial tuberosity. In these anomalies the high division occurs more often in the proximal than in the distal half of the arm, and the resulting arteries are often united by oblique anastomotic channels, while occasionally attenuated vasa aberrantia connect the axillary or brachial arteries with one or other of the forearm arteries (more frequently the radial). One or other of these anomalous branches may emerge through the deep fascia and run downwards subcutaneously.

Sometimes the brachial artery and median nerve forsake the cover of Biceps and run towards the medial epicondyle, usually passing behind a supracondylar process (or ligament) if it is present, or behind a band of fascia which gives rise to fibres of Pronator teres: this arrangement resembles that normally found in many carnivores.

Variations in the branches are not rare and one of the commonest is a joint origin for the profunda brachii and ulnar collateral arteries. In some specimens the latter artery runs anterior to the medial intermuscular septum; and rarely the ulnar collateral and posterior ulnar recurrent arteries are enlarged and constitute the first part of the ulnar artery, which then runs with the ulnar nerve behind the medial epicondyle; or a greatly enlarged ulnar collateral vessel may descend in front of the medial intermuscular septum to the anterior aspect of the medial epicondyle, before bending outwards to reach the cubital fossa where it replaces the ulnar artery. The median artery, which is usually a branch of the anterior interosseous, may spring from the brachial artery.

Collateral Circulation

If the brachial artery is tied in its proximal third the circulation is maintained by anastomoses between branches of the circumflex humeral, subscapular and acromiothoracic arteries with ascending branches of the profunda brachii and muscular branches of the brachial artery. If the arterial interruption is below the middle of the arm the circulation is carried on by the well developed anastomosis around the [illegible]

[illegible] posterior to the medial epicondyle, [illegible] anterior and posterior descending branches of the profunda brachii anastomosing in front of and behind the lateral epicondyle with the radial

The median nerve is lateral to the proximal part of the artery and the ulnar and medial cutaneous nerves of the arm and forearm are medial to it. The median nerve crosses the artery obliquely and lies medial to the distal part of the vessel, taking the place of the ulnar nerve which becomes separated from the artery by piercing the medial intermuscular septum alongside the ulnar collateral artery about the middle of the arm. Posteriorly the brachial artery lies successively on the long and medial heads of Triceps, the insertion of Coracobrachialis, and Brachialis; it is separated from the long head of Triceps by the radial nerve and the profunda brachii artery. There are two brachial venae comites and the basilic vein lies medial to the artery but separated from it, except in the upper part of the arm, by the deep fascia.

BRANCHES

The profunda brachii artery is a large branch which accompanies the radial nerve closely as it winds around the spiral groove of the humerus. On the lateral side of the arm it divides into two *descending branches* which run down anterior and posterior to the lateral intermuscular septum to the epicondylar region where they anastomose with the radial recurrent, supratrochlear and interosseous recurrent arteries. This profunda artery also supplies *muscular* branches to the Deltoid and to all three heads of the Triceps, a *nutrient* branch to the humerus which enters the bone near the deltoid insertion, an *ascending* branch which anastomoses with the posterior circumflex humeral artery, and a fine *collateral* twig which follows the nerve to the Anconeus and participates in the anastomosis around the elbow joint

The muscular branches are distributed to the Biceps, Coracobrachialis Triceps and Brachialis.

A nutrient branch supplies the humerus, entering a canal near the insertion of Coracobrachialis.

The ulnar collateral artery arises near the middle of the brachial artery It pierces the medial intermuscular septum alongside the ulnar nerve and descends with it to the interval between the medial epicondyle and the olecranon, where it ends under cover of Flexor carpi ulnaris by anastomosing with the ulnar recurrent and supratrochlear arteries.

The supratrochlear artery arises about two inches (5 cm) above the elbow and runs medially between the median nerve and the Brachialis, giving off branches which supply this muscle and anastomose with the ulnar collateral and anterior ulnar recurrent arteries. Piercing the medial intermuscular septum it turns outwards behind the humerus and deep to the Triceps to unite with the posterior descending branch of the profunda brachii and the interosseous recurrent arteries, and it also gives off branchlets behind the medial epicondyle which anastomose with the posterior ulnar recurrent and the collateral branch accompanying the nerve to Anconeus.

Variations

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Variations in the branches are not rare and one of the commonest is a joint origin for the profunda brachii and ulnar collateral arteries. In some specimens the latter artery runs anterior to the medial intermuscular septum; and rarely the ulnar collateral and posterior ulnar recurrent arteries are enlarged and constitute the first part of the ulnar artery, which then runs with the ulnar nerve behind the medial epicondyle; or a greatly enlarged ulnar collateral vessel may descend in front of the medial intermuscular septum to the anterior aspect of the medial epicondyle, before bending outwards to reach the cubital fossa where it replaces the ulnar artery. The median artery, which is usually a branch of the anterior interosseous, may spring from the brachial artery

Collateral Circulation

If the brachial artery is tied in its proximal third the circulation is maintained by anastomoses between branches of the circumflex humeral, subscapular and acromiothoracic arteries with ascending branches of the profunda brachii and muscular branches of the brachial artery If the arterial interruption is below the middle of the arm the circulation is carried on by the well developed anastomosis around the elbow joint This is formed by branches of the ulnar collateral and supratrochlear arteries anastomosing with the ulnar recurrent arteries anterior and posterior to the medial epicondyle, and by the anterior and posterior descending branches of the profunda brachii anastomosing in front of and behind the lateral epicondyle with the radial

and interosseous recurrent arteries. These are also united by transverse branches, the most definite forming an arch deep to the Triceps and above the olecranon fossa, which is joined by the twig accompanying the nerve to Anconeus.

THE ULNAR ARTERY

This is the larger terminal division of the brachial artery and it commences about the level of the upper border of the radial tuberosity. Running obliquely towards the medial side of the forearm it descends on the outer side of the ulnar nerve to the wrist where it divides into deep and superficial branches, the latter forming the main part of the superficial palmar arch.

Its proximal third lies deeply beneath Pronator teres, Flexor carpi radialis, Palmaris longus and Flexor digitorum sublimis and upon Brachialis and Flexor digitorum profundus. The median nerve is at first medial to the artery, but soon crosses over to its lateral side, being separated from the vessel by *the ulnar head of Pronator teres. The middle third is overlapped by* Flexor carpi ulnaris and lies on Flexor digitorum profundus; while the distal part lies on the same muscle, between Flexor carpi ulnaris and Flexor digitorum sublimis and covered only by the skin and fasciae. The ulnar nerve lies close to the medial side of the lower two-thirds of the artery and its palmar cutaneous branch lies in front of the terminal part of the artery.

At the wrist it is situated between the superficial and main parts of the flexor retinaculum, with the ulnar nerve and pisiform bone medially and the tendon of Palmaris longus laterally. It is accompanied by two venae comites and by the usual lymphatic channels and vascular nerves.

Branches

The ulnar recurrent arteries.—Both arise near the origin of the artery and the anterior is smaller than the posterior. The former gives twigs to Pronator teres and Brachialis and anastomoses with the ulnar collateral and supratrochlear arteries in front of the medial epicondyle. The latter runs *between the superficial and deep flexors* and ascends behind the medial epicondyle, deep to Flexor carpi ulnaris and close to the ulnar nerve, to anastomose with the ulnar collateral, supratrochlear and the interosseous recurrent arteries; it supplies the adjacent muscles and the elbow joint.

The common interosseous artery is a short stout branch which arises just below the level of the radial tuberosity and soon divides opposite the upper border of the antebrachial interosseous membrane into anterior and posterior divisions

The anterior interosseous artery runs downwards with the anterior interosseous nerve between Flexor digitorum profundus and Flexor pollicis longus on the front of the interosseous membrane, supplying these muscles and the radius and ulna. Near its origin it gives off the delicate *arteria mediana*

which accompanies the median nerve into the palm. It ends by bifurcating into two twigs, one of which joins the anterior carpal arch and the other pierces the interosseous membrane to anastomose with the corresponding posterior artery.

The posterior interosseous artery passes backwards between the oblique cord and the upper end of the interosseous membrane and then descends between the superficial and deep muscles on the back of the forearm as far as the wrist where it anastomoses with the termination of the anterior interosseous artery and the posterior carpal arch. Near its origin it gives off the interosseous recurrent artery which ascends through the Supinator and beneath Anconeus to behind the lateral epicondyle where it anastomoses with the supratrochlear and profunda brachii arteries.

Muscular offshoots from the main artery and its branches are distributed to the muscles along the ulnar side of the forearm.

Anterior and posterior carpal branches are small vessels which anastomose with corresponding branches of the radial artery, so forming delicate arches in front of and behind the wrist joint.

The deep (terminal) branch sinks between the Abductor and Flexor digiti minimi and, turning outwards, deep to the Opponens digiti minimi and the long flexor tendons and their sheaths, it joins the radial artery and so completes the *deep palmar arch*.

The superficial (terminal) branch forms the *main part of the superficial palmar arch* which is described below.

THE RADIAL ARTERY

This is the smaller subdivision of the brachial artery. It descends along the lateral side of the forearm to the wrist and then winds backwards through the anatomical snuff box before passing between the two heads of the first dorsal interosseous muscle into the palm where it unites with the deep branch of the ulnar, so forming the *deep palmar arch*.

The artery in the forearm is overlapped above by Brachioradialis, but its lower part is covered only by skin and fasciae. It rests successively on the tendon of Biceps, Supinator, Pronator teres, Flexor digitorum sublimis, Flexor pollicis longus, Pronator quadratus and the lower end of the radius. At the wrist it lies between the tendons of Flexor carpi radialis and Brachioradialis, the former intervening between the artery and the median nerve.

The superficial branch of the radial nerve is a lateral relation of the middle third of the artery, and lower down it is accompanied by filaments of the lateral antebrachial cutaneous nerve. It is also accompanied by the usual two venae comites, by lymphatic vessels and by vascular nerves.

As the artery winds backwards at the wrist it is crossed by the origin of the cephalic vein, some filaments of the radial nerve and by the tendons of Abductor pollicis longus, Extensor pollicis brevis, and Extensor pollicis

longus and it runs upon the lateral ligaments of the wrist joint, the scaphoid bone and the trapezium, before passing between the heads of the first dorsal interosseous muscle to reach the palm.

In the hand the artery turns medially, deep to the oblique head of Abductor pollicis and then between this and the transverse head of the muscle to unite with the deep branch of the ulnar artery and complete the *deep palmar arch.*

BRANCHES

The radial recurrent artery arises in the cubital fossa, runs between the radial nerve and its posterior interosseous branch, ascends beneath Brachioradialis and upon Supinator and Brachialis, supplying these muscles and the elbow joint, and anastomoses with the anterior descending branch of the profunda brachii artery.

Muscular branches are distributed to the muscles on the radial side of the forearm.

The anterior carpal branch is a slender vessel which unites with the corresponding branch of the ulnar artery to form the *anterior carpal arch;* this also receives a twig from the anterior interosseous artery and fine recurrent branches from the deep palmar arch.

The superficial palmar branch arises a short distance above the wrist and usually runs through and supplies the small thenar muscles, ending in them or by uniting with the superficial terminal ulnar branch to complete the *superficial palmar arch*

The posterior carpal branch arises in the region of the anatomical snuff box and runs medially beneath the extensor tendons on the dorsal surface of the carpus to anastomose with the corresponding branch of the ulnar artery and with terminal branches of the anterior and posterior interosseous arteries to form the *posterior carpal arch.* The *second, third and fourth dorsal metacarpal arteries* spring from this arch and descend on the corresponding dorsal interosseous muscles; they divide into two *dorsal digital arteries* for the supply of the adjacent sides of the fingers and anastomose with the palmar digital arteries. The dorsal metacarpal arteries communicate with the palmar vessels through proximal and distal *perforating branches* which run between the metacarpal bones.

The first dorsal metacarpal artery is given off as the artery is disappearing between the heads of the first dorsal interosseous muscle and it runs distally to supply the adjacent sides of the thumb and index finger. It may give off a branch to the postero-lateral aspect of the thumb, or this branch may arise directly from the radial artery.

The princeps pollicis artery arises as soon as the radial artery enters the palm and runs distally between the Adductor and Opponens pollicis and deep to the long flexor tendon of the thumb. About the level of the first metacarpophalangeal joint it divides into two branches which run along the palmar sides of the thumb and anastomose with the dorsal digital arteries.

The radialis indicis artery may arise directly from the radial or in common with the A. princeps pollicis, so forming the so-called *first palmar metacarpal artery*. It descends between the first dorsal interosseous muscle and the transverse head of Adductor pollicis and then along the radial side of the index finger to its tip, anastomosing with branches of the corresponding palmar digital branch on the ulnar side of the finger. It frequently sends a communication to the superficial palmar arch.

THE PALMAR ARCHES

The superficial palmar arch is chiefly formed by the superficial terminal branch of the ulnar artery and is usually completed by the superficial palmar branch of the radial artery, or by branches of the radialis indicis or princeps pollicis arteries It curves from the lateral side of the pisiform, across the hook of the hamate to the medial border of Flexor pollicis brevis, reaching the level of a line drawn across the palm from the distal border of the fully extended and abducted thumb. It is covered by the skin, superficial fascia and palmar aponeurosis and on the ulnar side by Palmaris brevis and it lies [illegible]

It supplies four *palmar digital branches*. The smallest and most medial is the proper palmar digital artery for the ulnar side of the little finger. The other three are larger and descend on the fourth, third and second lumbrical muscles towards the interdigital clefts where each divides into two palmar digital arteries for the supply of the contiguous sides of the little, ring and index fingers. They run behind the corresponding digital nerves and anastomose through dorsally directed twigs with the dorsal digital arteries. Just before each artery divides it is reinforced by a palmar metacarpal artery from the deep palmar arch Many glomera exist in connection with the small cutaneous vessels supplying the palmar aspects of the digits.

The deep palmar arch is about a half-inch (1·25 cm) proximal to the level of the superficial arch and is located deep to the long flexor tendons and their sheaths, the Lumbricals and the oblique head of Adductor pollicis, and upon the origin of the interossei muscles It is formed by the union of the terminal branch of the radial artery with the deep branch of the ulnar. The deep branch of the ulnar nerve runs outwards in the concavity of the arch.

It gives off three *palmar metacarpal* [illegible]

[illegible] clefts of the fingers. It also [illegible] three small *perforating branches* which pass backwards through the interosseous spaces to unite with the dorsal metacarpal arteries, and fine *recurrent branches* which ascend to end in the anterior carpal arch.

Variations in Arteries of Forearm and Hand

A number of abnormalities involving high origins or other anomalies of the radial, ulnar and interosseous arteries were mentioned when describing the axillary and brachial arteries and these will not be repeated, but it is worth remembering that the abnormal arteries often occupy superficial positions and so are more liable to injury or misplaced injections. Even when arising normally in the cubital fossa the arteries occasionally run distally superficial to the muscles.

The ulnar artery may be replaced by enlarged anterior interosseous or median arteries. Sometimes the latter arises directly from the axillary, brachial or ulnar arteries, and then it is unusually large and often ends by joining the superficial palmar arch or by dividing into one or more digital arteries. The common interosseous artery may spring from the radial artery and give off the radial recurrent branch, or the anterior and posterior interosseous vessels may arise separately from the ulnar artery.

The radial artery may be replaced in whole or part by branches of the ulnar or interosseous arteries and it may then end in the muscles of the forearm or in carpal and palmar branches. Or it may be normal, except that it winds backwards to the dorsum of the hand superficial instead of deep to the tendons. The princeps pollicis and radialis indicis branches may arise from a common trunk, or they may be absent and replaced by an enlarged dorsal digital artery to the index finger or by branches from the superficial palmar arch.

The palmar vascular arrangement is sometimes reversed, so that the radial and ulnar arteries respectively form the main parts of the superficial and deep palmar arches. One or other palmar arch may be absent (the superficial more often than the deep) and various anomalous vessels may end in them, such as enlarged median or interosseous arteries.

Collateral Circulation

The anastomoses around the elbow and wrist joints and between the various muscular, interosseous, carpal, palmar and other branches are so free that ligature of both radial and ulnar arteries, or even of the distal part of the brachial artery, seldom results in gangrene. Indeed the communications are so free that bleeding from palmar arch wounds creates well-known surgical problems if for any reason the vessels cannot be secured locally.

THE ABDOMINAL AORTA

This vessel is discussed in a book on peripheral vascular diseases for reasons that will become evident to readers of the clinical sections

It extends from the aortic opening in the Diaphragm opposite the last thoracic vertebra, to end slightly to the left of the mid-line on the body of

the fourth lumbar vertebra by dividing into the two common iliac arteries. It is retroperitoneal and from above downwards it lies behind the liver, stomach, body of pancreas, third part of duodenum, the root of the mesentery and coils of small gut. It is also posterior to the coeliac, intermesenteric and superior hypogastric autonomic plexuses, to the splenic and left renal veins, and to certain of its own branches such as the coeliac and mesenteric arteries It lies on the upper four lumbar vertebrae and the corresponding intervertebral disks and ligaments, with the lower two or three left lumbar veins intervening as they pass across to join the inferior vena cava, and it may partly overlap the anterior border of the left Psoas major. The inferior vena cava lies on its right side, but is separated above from the artery by the cisterna chyli, thoracic duct, azygos vein, right coeliac ganglion and the right crus of the Diaphragm On the left side it is related to the left crus of the Diaphragm, the left coeliac ganglion, the duodeno-jejunal flexure, coils of small gut, and the left sympathetic ganglionated trunk. Aortic lymph nodes lie on its anterior and lateral sides.

BRANCHES

Before bifurcating into the common iliac arteries the abdominal aorta gives off (1) numerous **visceral** arteries *which need only be enumerated here*—coeliac, superior mesenteric, inferior mesenteric, suprarenal, renal, gonadic (testicular and ovarian), and (2) a number of mainly **parietal** branches—phrenic, lumbar and median sacral.

The phrenic arteries are small and variable and are distributed mainly to the Diaphragm They anastomose with the intercostal, musculophrenic, suprarenal and pericardiacophrenic arteries.

The lumbar arteries are in series with the aortic intercostal arteries, and there are commonly four pairs; a fifth pair may arise from the median sacral artery, but they are often represented by the lumbar branches of the ilio-lumbar arteries. They run outwards and backwards on the bodies of the lumbar vertebrae [illegible]

to the Ps [illegible]

to the [illegible] the intervals between the transverse processes they are continued into the abdominal wall, the upper three arteries passing behind Quadratus lumborum and the fourth often in front. Beyond the outer border of this muscle they run between the internal oblique and transverse abdominal muscles, supplying them and finally anastomosing with each other, and with the lower intercostal, phrenic, subcostal, iliolumbar, deep circumflex iliac and inferior epigastric arteries. In the retroperitoneal tissues they also form numerous fine connections with branches of the mesenteric (jejunal, ileal, colic), hepatic and renal arteries.

Each artery gives off a largish *posterior* branch which is homologous with the corresponding branch of a posterior intercostal artery and is distri-

buted to the muscles and skin of the back, and through a spinal offshoot to structures within the vertebral canal.

The median sacral artery, a small and unpaired vessel, arises from the posterior aspect of the aorta just above its termination and descends anterior to the lumbosacral junction, sacrum and coccyx to end by supplying the coccygeal glomus. It often gives off a fifth pair of *lumbar* arteries (*q.v.*), minute *spinal* branches, fine *parietal* branches which run outwards to anastomose with the iliolumbar and lateral sacral arteries, and delicate *rectal* twigs which anastomose with the superior and middle rectal arteries.

VARIATIONS

Variations in the abdominal aorta are uncommon. Its length is determined by the extent of fusion of the two primitive dorsal aortae. Sometimes this extends as low as the last lumbar vertebra, or it may be less than usual and the bifurcation is then at the level of the third or even of the second lumbar vertebra; the lengths of the common iliac arteries are shorter or longer in consequence. Sometimes the common iliac artery is absent on one or both sides and then the internal and external iliac arteries arise directly from the aorta; this resembles the common arrangement in many other mammals. Very rarely the two primitive aortae persist, or their adjacent walls fail to become absorbed in whole or in part and remain as a more or less complete septum along the vessel, a condition which may be associated with zones of coarctation, although localised narrowing may exist in an otherwise normal aorta.

COLLATERAL CIRCULATION

Sudden occlusion of the upper half of the abdominal aorta deprives vital organs such as the liver, pancreas, kidneys and suprarenals of their blood supply and no adequate natural collateral channels exist to counteract such a catastrophe, although very occasionally it may be circumvented by prompt surgical intervention. If the occlusion is more gradual there may be time for the development of a collateral circulation, because there are extensive interconnections between the various branches of the coeliac and mesenteric arteries along the length of the gastro-intestinal tract; and others between the vessels of the liver, pancreas, kidneys, suprarenals, small intestines, colon and rectum and parietal vessels such as branches of the intercostal, subcostal, phrenic, epigastric, lumbar, iliolumbar, gluteal, lateral sacral, median sacral and internal pudendal arteries. These parieto-visceral anastomoses are numerous but normally insignificant in size, although when given time to distend they may prove sufficient to sustain an adequate collateral circulation

If the lower part of the aorta is blocked, below the origin of the inferior mesenteric artery, multiple collateral channels may enlarge and maintain the blood supply to pelvic and lower limb structures. The chief of these anastomoses are:—

(1) Those above-mentioned between branches of the coeliac and mesenteric arteries, and between them and the arteries of the solid viscera and adjacent parietal vessels.

(2) Between the upper and lower lumbar arteries; and between them and branches of the intercostal, subcostal, phrenic, iliolumbar, median sacral, gluteal, circumflex iliac and inferior epigastric arteries.

(3) Between the superior epigastric and musculophrenic branches of the internal mammary artery and the inferior epigastric and deep circumflex iliac branches of the external iliac artery.

(4) Between the colic and rectal branches of the inferior mesenteric artery and the rectal branches of the internal iliac, internal pudendal, median sacral and inferior gluteal arteries.

(5) Between the testicular arteries and the vesical, vesiculo-deferential, cremasteric, circumflex iliac and internal and external pudendal arteries *in the male*; and between the ovarian, tubal, uterine, vesical, circumflex iliac and internal and external pudendal arteries *in the female*.

THE COMMON ILIAC ARTERIES

These are formed by the bifuraction of the aorta and each is approximately two inches (5 cm.) in length, the right being slightly longer than the left. They diverge, each passing in the direction of the front of the ipsilateral sacro-iliac joint, where it divides into **external and internal iliac arteries.**

These arteries are retroperitoneal, and lie on the lower part of the lumbar spine and lumbosacral junction, the sympathetic trunks and the psoas muscles. The right artery also lies on the terminations of both common iliac veins as they unite to form the inferior vena cava. The left vein lies inferomedial to the artery.

The superior hypogastric plexus (pre-sacral nerve) descends in the interval between the diverging vessels, and each artery is crossed near its termination by the corresponding ureter. The left artery is also crossed by the superior rectal vessels

Branches

Normally the external and internal iliac arteries are the only branches of the common iliac arteries, though occasionally they give rise to one or more of the iliolumbar, sacral, gonadic or ureteric arteries, and they are rare sources of accessory renal arteries.

Collateral Circulation

This is virtually the same as for blockage of the lower part of the abdominal aorta (see above).

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Collateral Circulation

Sudden occlusion of the upper half of the abdominal aorta deprives vital organs such as the liver, pancreas, kidneys and suprarenals of their blood supply and no adequate natural collateral channels exist to counteract such a catastrophe, although very occasionally it may be circumvented by prompt surgical intervention. If the occlusion is more gradual there may be time for the development of a collateral circulation, because there are extensive interconnections between the various branches of the coeliac and mesenteric arteries along the length of the gastro-intestinal tract, and others between the vessels of the liver, pancreas, kidneys, suprarenals, small intestines, colon and rectum and parietal vessels such as branches of the intercostal, subcostal, phrenic, epigastric, lumbar, iliolumbar, gluteal, lateral sacral, median sacral and internal pudendal arteries. These parieto-visceral anastomoses are numerous but normally insignificant in size, although when given time to distend they may prove sufficient to sustain an adequate collateral circulation.

If the lower part of the aorta is blocked, below the origin of the inferior mesenteric artery, multiple collateral channels may enlarge and maintain the blood supply to pelvic and lower limb structures The chief of these anastomoses are:—

arteries to form the *cruciate anastomosis*. Any or all of these normally slender branches may become dilated and tortuous if the femoral or popliteal arteries become blocked for any reason.

THE POSTERIOR TRUNK.—The posterior trunk of the internal iliac artery gives off iliolumbar and lateral sacral branches and ends as the superior gluteal artery.

The iliolumbar artery runs upwards and outwards in front of the sacro-iliac joint and lumbosacral trunk and divides near the medial border of Psoas major into *lumbar* and *iliac* branches. The former supplies the Psoas major and the Quadratus lumborum and anastomoses with the deep circumflex iliac and lumbar arteries. The latter ramifies widely in the iliac fossa, supplying Iliacus and the hip bone, and anastomosing with branches of the obturator, deep circumflex iliac, superior gluteal and lateral circumflex femoral arteries

The lateral sacral arteries, superior and inferior, supply structures in the sacral region, some branches passing through the sacral foramina to reach the lower back. They anastomose with branches of the gluteal and median sacral arteries

The superior gluteal artery is the largest branch of the internal iliac artery and it pierces the pelvic fascia, passes backwards between the lumbosacral trunk and the first sacral nerve, and enters the gluteal region by passing through the upper part of the greater sciatic foramen above Piriformis. Within the pelvis it supplies Piriformis, Obturator internus and the hip bone, and soon after emerging it divides into superficial and deep branches. The *superficial branch* ramifies at once and most of its subsidiary branchings supply Gluteus maximus and the skin over it, anastomosing with branches of the inferior gluteal and lateral sacral arteries The *deep branch* passes between Gluteus medius and Gluteus minimus, supplying them and the hip bone Usually it divides into upper and lower divisions; the former follows the upper border of Gluteus minimus towards the anterior superior iliac spine where it unites with the deep circumflex iliac and lateral circumflex femoral arteries. The latter runs near the superior gluteal nerve and crosses the Gluteus minimus towards the great trochanter, anastomosing with branches of the inferior gluteal and circumflex femoral arteries.

THE EXTERNAL ILIAC ARTERY

This artery is about four inches (10 cm) long and extends from the bifurcation of the common iliac artery to the level of the inguinal ligament. It runs downwards, forwards and outwards along the medial border of Psoas major, and at its termination it lies midway between the anterior superior iliac spine and the symphysis pubis.

It lies upon the fascia iliaca, and external to the peritoneum which separates it from the small and large intestines. The ureter crosses it at its

THE INTERNAL ILIAC ARTERY

This artery arises in front of the sacro-iliac joint and passes to the upper margin of the greater sciatic foramen where it divides into anterior and posterior trunks. It lies behind the peritoneum and is crossed by the ureter; behind it are the internal iliac vein, the lumbosacral nerve trunk and the sacro-iliac joint.

THE ANTERIOR TRUNK.—The branches from the anterior trunk are mainly visceral or supply the genitalia, such as the *superior* and *inferior vesical* and *vesiculo-deferential arteries*, the *middle rectal* and *internal pudendal arteries*, and the *uterine* and *vaginal arteries* in the female. Others, such as the obturator and inferior gluteal arteries, are mainly or entirely parietal in distribution.

The obturator artery hugs the lateral pelvic wall, running towards and through the upper part of the obturator foramen into the thigh. It is in contact laterally with the obturator fascia covering the Obturator internus and is crossed medially by the ureter and vas deferens which separate it from the peritoneum The obturator nerve and vein are above and below the artery respectively.

Within the pelvis it gives off *iliac* branches to the Iliacus and the ilium, which anastomose with the iliolumbar artery; a *vesical* branch; and a *pubic* branch which ramifies behind the pubis, anastomosing with its fellow and with the pubic branch of the inferior epigastric artery In about one in four individuals this last-named branch replaces the obturator artery, and this abnormal vessel may descend along either the lateral or medial margin of the femoral ring and so be endangered in certain hernial operations.

The main obturator artery divides into *anterior and posterior branches* as soon as it enters the thigh and these encircle the margins of the obturator foramen, supplying the adjacent muscles, bone and hip joint, and anastomosing with each other and with the medial circumflex femoral and inferior gluteal arteries

The inferior gluteal artery is larger than the internal pudendal, which is the other terminal branch of the anterior trunk of the internal iliac artery It descends on the sacral plexus and Piriformis, supplies a few twigs to the rectum, and then runs between the first and second or second and third sacral nerves and between Piriformis and Coccygeus before leaving the pelvis through the greater sciatic foramen. On entering the gluteal region it runs posteromedial to the sciatic nerve, deep to Gluteus maximus, and behind the Obturator internus, Gemelli and Quadratus femoris to reach the upper part of the thigh, giving off numerous branches to the buttock muscles and to the upper ends of the hamstrings. Other branches supply the *coccygeal* region, and it provides the slender *arteria comitans* of the sciatic nerve and fine *cutaneous* branches which accompany those of the posterior cutaneous nerve of the thigh. One *anastomotic* branch usually supplies a twig to the hip joint, and joins with the first perforating and medial and lateral femoral circumflex

division of the internal iliac artery beyond the origin of the superior vesical artery (the part forming the foetal umbilical artery). Occasionally the external iliac gives off some of the uppermost branches normally given off by the femoral artery, or vice versa, or its inferior epigastric branch may be replaced by enlargement of the pubic branch of the obturator artery. The arteria profunda femoris may arise above the inguinal ligament and a small additional aberrant vessel, running either anterior or posterior to the inguinal ligament, sometimes interconnects the external iliac and femoral arteries.

Collateral Circulation

After ligature of the external iliac artery the circulation is re-established through the numerous anastomoses between the iliolumbar, lateral sacral, muscular, pudendal, obturator and gluteal branches of the internal iliac artery, the deep circumflex iliac, muscular and inferior epigastric branches of the external iliac artery, and the circumflex femoral, external pudendal, superficial epigastric, circumflex iliac and profunda branches of the femoral artery. Other communications also enlarge between the superior and inferior epigastric arteries and between the superficial and deep circumflex iliac, lumbar and intercostal arteries.

THE FEMORAL ARTERY

This is the chief stem artery of the lower limb and it extends from behind the inguinal ligament to the opening in Adductor magnus where it becomes the popliteal artery Its proximal half lies in the femoral triangle and the distal part in the subsartorial (Hunter's) canal. The uppermost one-and-a-half inches (3·7 cm.) of both artery and vein are enclosed in the femoral sheath, a funnel-shaped fascial investment divided by fibrous septa into three compartments, the lateral being occupied by the femoral artery, the intermediate by the vein, and the medial (the femoral canal) by lymphatic vessels and a lymph node.

Above, the artery is covered only by skin and fasciae, the superficial inguinal lymph nodes, small vessels, and the medial femoral cutaneous nerve; lower down it is also covered by Sartorius and by the fascial roof of the subsartorial canal. Posterior to it are the Psoas major, Pectineus, Adductor longus and Adductor magnus. The nerve to Pectineus passes behind it, and the femoral vein and profunda femoris artery lie between it and Pectineus. Inferiorly the vein is lateral to the artery, but it passes behind the artery to gain its medial side above. Lateral to the upper part of the artery are the Sartorius, the femoral nerve and the femoral branch of the genitofemoral nerve, and lower down are the saphenous nerve and the Vastus medialis and its nerve The saphenous nerve crosses the artery anteriorly and near its termination lies on its medial side.

origin, and in the female the ovarian vessels run over it at a slightly lower level, while the testicular vessels lie for some distance upon it near its termination. This part of the artery is crossed by the genital branch of the genitofemoral nerve, the deep circumflex iliac vein, the vas deferens in the male, and the round ligament of the uterus in the female. The external iliac vein is medial to the distal part of the artery and posterior to its upper part, and both vessels are enclosed in a common fascial sheath. A chain of lymph nodes and vessels lies in front and at the sides of the vessels.

Branches

The external iliac artery gives off two named branches, besides twigs to the Psoas major and to the adjacent lymph nodes.

The inferior epigastric artery arises immediately above the inguinal ligament, or abnormally from the femoral artery just beyond the ligament. It ascends in the extraperitoneal tissue along the medial margin of the deep inguinal ring, pierces the transversalis fascia, passes in front of the arcuate line and so enters the Rectus abdominis sheath. It soon penetrates the muscle, dividing into numerous branches which supply it and the neighbouring tissues and skin and form anastomoses with the superior epigastric branch of the internal mammary artery and branches of the posterior interosseous and lumbar arteries.

Near its origin it gives off a *cremasteric* twig which supplies the Cremaster and other structures in the spermatic cord, and a *pubic* branch which in about one in four persons is enlarged to form an *abnormal obturator artery*. Much less often the pubic branch of the obturator artery is enlarged and replaces the normal inferior epigastric artery. In the female a small branch supplies the round ligament of the uterus and replaces the cremasteric branch.

The deep circumflex iliac artery also arises immediately above the inguinal ligament and runs obliquely upwards and outwards in a delicate sheath formed by the union of the transversalis and iliac fascia. In the vicinity of the anterior superior iliac spine it pierces the fascia and the Transversus abdominis and then runs between it and the Obliquus internus to end by anastomosing with branches of the iliolumbar and superior gluteal arteries. It also anastomoses with branches of the lateral circumflex femoral and superficial circumflex iliac arteries near the anterior superior iliac spine, and hereabouts it sends off an *ascending branch* between the transverse and internal oblique abdominal muscles, which supplies them and other parietal structures and anastomoses with branches of the lumbar, lower intercostal and inferior epigastric arteries.

Variations

Very rarely the inferior gluteal artery persists as the main supply of the lower limb and then the external iliac artery is rudimentary. Even more uncommon is persistence of the normally obliterated portion of the anterior

division of the internal iliac artery beyond the origin of the superior vesical artery (the part forming the foetal umbilical artery). Occasionally the external iliac gives off some of the uppermost branches normally given off by the femoral artery, or vice versa, or its inferior epigastric branch may be replaced by enlargement of the pubic branch of the obturator artery. The arteria profunda femoris may arise above the inguinal ligament and a small additional aberrant vessel, running either anterior or posterior to the inguinal ligament, sometimes interconnects the external iliac and femoral arteries.

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Branches

The most important branch is the *profunda femoris* and it is described separately after the others.

The first four smallish branches arise from the proximal inch of the artery and pierce the femoral sheath.

The superficial epigastric artery passes through the saphenous opening and ascends on the abdominal wall, anastomosing with branches of the inferior and superior epigastric arteries, and with other neighbouring branches of the femoral artery.

The superficial circumflex iliac artery pierces the fascia lata and runs in the superficial fascia towards the anterior superior iliac spine, supplying the skin, fasciae, adjacent lymph nodes, Sartorius and Tensor fasciae latae. It anastomoses with the deep circumflex iliac, superior gluteal and lateral circumflex arteries.

The superficial external pudendal artery runs through the saphenous opening, over the spermatic cord (or round ligament) and supplies the superficial structures in the lower abdominal wall and the adjacent parts of the genitalia. It anastomoses with its fellow, with the superficial epigastric and deep external pudendal vessels, and with the terminal branches of the internal pudendal arteries.

The deep external pudendal artery lies under the fascia lata, which it pierces to reach the external genitals. Its anastomoses are similar to those of the superficial external pudendal artery.

The descending genicular artery arises near the termination of the femoral artery and divides into a *superficial* branch which runs with the saphenous nerve for a variable distance and a *deep* branch which enters Vastus medialis, supplies it, and joins the anastomosis around the knee joint.

Muscular branches. — Apart from those muscular branches already mentioned, a variable number of muscular twigs are given off directly from the main femoral artery to neighbouring muscles such as Sartorius, Quadriceps femoris and the Adductors.

THE ARTERIA PROFUNDA FEMORIS.—The profunda femoris is the largest branch of the femoral artery and is the principal supply of the adductor, extensor and hamstring muscles. It arises from the postero-lateral aspect of the femoral artery one-and-a-half inches to two inches (3·7 - 5 cm.) below the inguinal ligament. It inclines medially, descending upon Iliacus, Pectineus, Adductor brevis and Adductor magnus, and is separated from the main artery by Adductor longus and by the femoral and profunda veins. It ends as the fourth perforating artery. It gives off lateral and medial circumflex and perforating branches.

The lateral circumflex artery runs outwards on Iliacus, beneath Rectus femoris and Sartorius, and between the divisions of the femoral nerve. It divides into ascending, transverse and descending branches. The *ascending*

branch runs up beneath Rectus femoris and Tensor fasciae latae, helping to supply them and the hip joint and anastomosing with the deep circumflex iliac and gluteal arteries. The *transverse branch* courses outwards round the femur between Rectus femoris and Vastus intermedius, pierces Vastus lateralis, and anastomoses below the trochanter with branches of the medial circumflex, inferior gluteal and first perforating arteries (*cruciate anastomosis*). The *descending branch* follows the nerve to Vastus lateralis and anastomoses with twigs of the perforating arteries and genicular branches of the femoral and popliteal arteries.

The medial circumflex artery runs between Psoas major and Pectineus, below the hip joint, and between Adductor brevis and Obturator externus to the upper border of Adductor magnus where it ends in ascending and transverse branches. Besides these it supplies twigs to all the nearby muscles and to the hip joint. The *ascending branch* passes between Obturator externus and Quadratus femoris to the trochanteric fossa where it anastomoses with branches of the gluteal arteries. The *transverse branch* helps to form the *cruciate anastomosis* mentioned above

The perforating branches pass through openings in Adductor magnus to reach the back of the thigh and there are usually four, including the terminal branch of the profunda They curve round close to the femur and all end in the Vastus lateralis. They are irregular, but the following is a common arrangement· the *first* winds between Pectineus and Adductor brevis, through Adductor magnus and into Vastus lateralis and forms part of the *cruciate anastomosis;* the *second* perforates both the short and great adductors and then passes between Gluteus maximus and the short head of Biceps into Vastus lateralis, supplying these and a nutrient branch to the femur; the *third* arises at the lower border of Adductor brevis and runs through Adductor magnus and the short head of Biceps into Vastus lateralis; and the *fourth*, the termination of the profunda artery, runs a similar course at a somewhat lower level All the perforating arteries anastomose freely with each other, with branches of the gluteal and circumflex arteries above, and with muscular and genicular branches of the femoral and popliteal arteries below.

VARIATIONS

Variations in the origins of the proximal branches were ment[illegible]
discussing the [illegible]
ove[illegible]
art[illegible] the femoral artery is small and ends in the thigh as the profunda femoris. The profunda artery may arise either distal or proximal to its usual position and sometimes it crosses in front of the artery and vein, or it may be absent and then its branches arise directly from the main artery In several mammals a long saphenous artery, arising near the profunda artery, accompanies the corresponding nerve to the medial side of the foot, and this vessel has been recorded as occurring in man.

Collateral Circulation

If the femoral artery is tied above its profunda branch the circulation is maintained chiefly by anastomoses between branches of the superior and inferior gluteal, the medial and lateral circumflex and the first perforating arteries; between the obturator and femoral circumflex arteries; between the external and internal pudendal arteries; and between the deep circumflex iliac and lateral femoral circumflex arteries.

If the artery is tied below the profunda branch the circulation is maintained by anastomoses between the inferior gluteal, medial and lateral femoral circumflex and perforating arteries with muscular and genicular branches of the femoral and popliteal arteries.

THE POPLITEAL ARTERY

This is the continuation of the femoral artery and extends from the opening in Adductor magnus to the lower border of Popliteus where it divides into *anterior and posterior tibial arteries.*

It lies in the popliteal fossa, surrounded by a variable amount of fat, and it is covered by the Semimembranosus above and by the Gastrocnemius and Plantaris below. The artery lies behind the lower end of the femur, the back of the knee joint and the fascia over Popliteus. The medial popliteal nerve and the popliteal vein are lateral to the upper part of the artery, but they cross it superficially, the vein intervening between the artery and the nerve, and lie medial to its lower part. A number of lymph nodes are arranged around the artery and in its distal part it is crossed by the nerves to Popliteus and Soleus

Branches

Cutaneous branches supply the skin and fasciae over the popliteal fossa and the calf of the leg.

Muscular branches.—An upper group supply the lower parts of the hamstring and adductor magnus muscles, and anastomose with branches of the profunda artery. The lower muscular or *sural* arteries are distributed to the proximal parts of the calf muscles

Genicular branches, five in number, are arranged as superior and inferior pairs, with a middle unpaired vessel. They supply twigs to the knee joint and to the adjacent muscles and bones and form a profuse anastomosis around the knee joint.

The medial superior genicular artery runs under Semimembranosus, Semitendinosus and the tendon of Adductor magnus, above the medial head of Gastrocnemius. It supplies Vastus medialis and anastomoses with the descending, medial inferior and lateral superior genicular arteries.

The lateral superior genicular artery passes laterally above the lateral condyle and deep to the tendon of Biceps femoris. It supplies Vastus lateralis

and anastomoses with the descending branch of the lateral femoral circumflex artery, and with the medial superior and lateral inferior genicular arteries.

The medial inferior genicular artery runs *deep to the medial head* of Gastrocnemius, along the upper border of Popliteus, and continues between the medial tibial condyle and the medial ligament of the knee. It supplies the adjacent osseous, articular and muscular structures and anastomoses with its fellow of the opposite side, with the anterior and posterior tibial recurrent arteries and with the medial superior genicular artery.

The lateral inferior genicular artery courses outwards across Popliteus and deep to Plantaris and the lateral head of Gastrocnemius. It curves forwards above the head of the fibula, beneath the tendon of Biceps femoris and the lateral ligament of the knee, and ends by anastomosing with the lateral superior and medial inferior genicular arteries and with the circumflex fibular and anterior and posterior tibial recurrent arteries.

The middle genicular artery is a small vessel arising opposite the back of the knee joint It pierces the posterior capsular ligaments and supplies twigs to the cruciate ligaments, synovial membrane and femoral condyles.

VARIATIONS

When the external iliac and femoral arteries are rudimentary (*q.v.*) the popliteal may be the direct continuation of the inferior gluteal artery: this is a rare anomaly. Occasionally the popliteal artery is duplicated in part, or it may divide into the anterior and posterior tibial arteries at a more proximal or more distal level than usual. Sometimes it divides into three branches, the additional one being the peroneal artery; and rarely the posterior tibial artery is small or absent and is largely replaced by a peroneal artery arising as one of the terminal branches of the popliteal. One of the popliteal cutaneous branches accompanying the short saphenous vein may be enlarged to form a *short saphenous artery*, or one of these branches may run superficially for a variable distance before passing deeply again to join the posterior tibial artery

COLLATERAL CIRCULATION

This varies with the site of occlusion or ligature and although theoretically many vessels are available to carry on the circulation, particularly those entering into the free anastomosis around the knee joint described above, in practice surgeons prefer to ligate the femoral artery in the subsartorial (Hunter's) canal.

In general the descending genicular, the terminal branches *of the* perforating arteries and the descending branch of the lateral femoral circumflex *anastomose with the* superior muscular and genicular branches of the popliteal, and these in turn communicate freely with the inferior genicular and muscular branches of the popliteal and with the anterior and posterior tibial recurrent and circumflex fibular arteries.

THE POSTERIOR TIBIAL ARTERY

This is the larger terminal branch of the popliteal artery and it extends downwards from the lower border of the Popliteus to end midway between the medial malleolus and the medial tubercle of the calcaneum, and beneath the flexor retinaculum, by dividing into the *medial and lateral plantar arteries.*

It lies between the superficial and deep muscles, namely beneath Gastrocnemius, Soleus and the deep transverse fascia of the leg, and upon Tibialis posterior, Flexor digitorum longus, the tibia and the posterior ligament of the ankle joint. Its distal part is superficial, being covered only by the skin and fasciae, and it runs parallel to and about one inch (2·5 cm.) in front of the medial border of the tendo calcaneus. The posterior tibial nerve lies at first medial to the artery but soon crosses it posteriorly and is continued downwards on its lateral side. The artery has two venae comites.

BRANCHES

These are circumflex fibular, cutaneous, muscular, peroneal, nutrient, communicating, calcanean and malleolar. The peroneal is the largest branch and for convenience is described last, although in fact it is one of the first branches.

The circumflex fibular artery is small and curves round the neck of the fibula and through Soleus to anastomose with the inferior genicular and anterior tibial recurrent arteries.

Cutaneous twigs supply the skin of the postero-medial surface of the leg.

Muscular branches supply all the adjacent muscles.

A nutrient vessel enters the nutrient canal of the tibia

A communicating branch unites the posterior tibial and peroneal arteries about two inches (5 cm.) above the lower end of the tibia.

The calcanean branches arise from the terminal part of the posterior tibial and supply the medial and posterior parts of the heel, anastomosing with branches of the peroneal and medial malleolar arteries.

The malleolar branch(es) supplies the tissues in the region of the medial malleolus and aids in forming the medial malleolar network.

THE PERONEAL ARTERY.—The peroneal artery arises about one inch (2·5 cm) below the origin of the posterior tibial artery. It inclines outwards across Tibialis posterior towards the fibula and then descends between Tibialis posterior and Flexor hallucis longus. Passing behind the inferior tibio-fibular joint and lateral malleolus it ends by supplying the lateral side of the heel and ankle.

It provides *muscular* branches for Soleus, Tibialis posterior, Flexor hallucis longus and the Peronei; a *nutrient* artery to the fibula; a *communicating* branch which joins the corresponding branch from the posterior tibial artery; a *perforating* branch which reaches the front of the leg by piercing the interosseous membrane about two inches (5 cm.) above the lateral malleolus

and thereafter runs anterior to the ankle to the dorsum of the foot, supplying branches to the ankle and inferior tibio-fibular joints and to Peroneus tertius and the tarsus; and *malleolar* and *calcanean* branches which supply the lateral side of the ankle and heel and anastomose with the other *malleolar* and calcanean arteries arising from the tibial, plantar and tarsal arteries.

PLANTAR ARTERIES

The medial and lateral plantar arteries arise beneath the flexor retinaculum and the origin of Abductor hallucis as the terminal divisions of the posterior tibial artery.

The medial plantar artery is small and passes along the medial side of the foot, medial to the medial plantar nerve, and between Abductor hallucis and Flexor digitorum brevis It unites with the digital branch of the first plantar metatarsal artery and the joint vessel supplies the medial side of the great toe In its course it supplies the adjacent muscles, joints and skin and gives off three small *superficial digital* branches which anastomose, at the level of the interdigital clefts, with the first, second and third plantar metatarsal arteries

The lateral plantar artery is larger and runs outwards and forwards on the lateral side of the lateral plantar nerve, lying consecutively between Abductor hallucis and the calcaneum, Flexor digitorum brevis and Flexor digitorum accessorius, and Flexor digitorum brevis and Abductor digiti minimi.

About level with the base of the fifth metatarsal bone it curves medially to the interval between the bases of the first and second metatarsal bones where it joins the dorsalis pedis artery, so completing the **plantar arch.** This arch lies deeply beneath the bases of the second, third and fourth metatarsals and of the origins of the corresponding interossei, and above the oblique head of Adductor hallucis

The lateral plantar artery gives off *calcanean* branches to the outer side of the heel; *cutaneous, muscular* and *articular* branches to adjacent structures; and *anastomotic* branches which unite with the lateral malleolar, lateral tarsal and arcuate arteries.

The plantar arch gives off four plantar metatarsal and three perforating branches The *plantar metatarsal arteries* run forwards on the plantar aspects of the Interrossei and each divides into a pair of *plantar digital arteries* which supply the adjacent sides of the toes, and the first one also sends a digital branch to the medial side of the big toe which unites with the *termination* of the medial plantar artery. Near their points of division each gives off a small *anterior perforating* branch which runs upwards to join the corresponding dorsal metatarsal artery. The plantar digital artery *to the lateral* side of the little toe arises independently from the lateral plantar artery at the point where it bends medially to form the plantar arch. The three (posterior)

perforating branches pass upwards between the heads of the dorsal Interosse and unite with the dorsal metatarsal arteries.

THE ANTERIOR TIBIAL ARTERY

This is the smaller of the two terminal divisions of the popliteal artery and it begins on the back of the leg at the lower border of Popliteus. Passing forwards to the front of the leg between the two heads of Tibialis posterior and through an opening in the uppermost part of the interosseous membrane, it turns downwards and extends to the level of the ankle joint where it changes its name and is continued as the *arteria dorsalis pedis.*

In its upper two-thirds it is in contact with the anterior surface of the interosseous membrane, and it is overlapped by the Tibialis anterior medially and by the Extensor digitorum longus and Extensor hallucis longus laterally. In its lower third it rests upon the front of the tibia and the anterior ligament of the ankle, and it is relatively superficial, being covered by the skin, fasciae and superior extensor retinaculum. The anterior tibial nerve as it descends lies at first lateral, then anterior, and again lateral to the artery. The tendon of Extensor hallucis crosses over the artery from the lateral to the medial side about the level of the ankle, so that the artery lies between this tendon and that of Extensor digitorum longus, with the anterior tibial nerve intervening between the artery and the first long digital tendon. The artery usually has two venae comites.

Branches

The posterior tibial recurrent artery is small and inconstant and is given off before the main artery passes through the interosseous membrane. It runs upwards in front of Popliteus, supplies it and the superior tibio-fibular joint, and anastomoses with the inferior genicular arteries.

The anterior tibial recurrent artery arises immediately after the artery has passed through the interosseous membrane. It pierces and supplies Tibialis anterior and anastomoses with the genicular and circumflex fibular arteries.

Cutaneous branches supply the skin of the front of the leg.

Muscular branches are distributed to the adjacent muscles.

The anterior medial malleolar artery arises near the lower end of the artery, passes behind the tendons of Extensor hallucis longus and Tibialis anterior, and assists in forming a *medial malleolar network* by anastomosing with the malleolar and calcanean branches of the posterior tibial artery, the medial tarsal branches of the dorsalis pedis artery, and twigs from the medial plantar artery.

The anterior lateral malleolar artery runs outwards beneath the tendons of the Extensor digitorum longus and Peroneus tertius and assists in forming a *lateral malleolar network* by anastomosing with the perforating and calcanean branches of the peroneal artery, branches from the lateral plantar artery, and the lateral tarsal branch of the arteria dorsalis pedis These

malleolar networks supply the cutaneous, fascial, osseous and articular structures in the region of the ankle joint.

THE DORSALIS PEDIS ARTERY

This is the continuation of the anterior tibial artery. It runs along the medial and dorsal aspect of the foot to the proximal end of the first intermetatarsal space where it gives off the first dorsal metatarsal artery before descending into the sole between the heads of the first dorsal interosseous muscle to complete the *plantar arch* by uniting with the lateral plantar artery.

It is covered by the skin, fasciae and inferior extensor retinaculum and is crossed by the tendon of the Extensor brevis passing to the big toe. The tendon of Extensor hallucis longus lies medial to it, and on its lateral side are the first tendon of Extensor digitorum longus and the medial terminal branch of the anterior tibial nerve. It rests successively upon the anterior ligament of the ankle joint, the talus, the navicular and the second cuneiform bones and their interconnecting ligaments. Two venae comites accompany the artery.

Branches

The tarsal arteries arise as the artery crosses the talus or navicular, and there are several small ones on both the lateral and medial sides. One of the lateral vessels is larger than the others and runs outwards to supply Extensor digitorum brevis and the tarsal articulations These arteries anastomose with branches of the anterior and posterior tibial, peroneal, arcuate, and medial and lateral plantar arteries, and they assist in forming the malleolar networks described above

The arcuate artery is given off as the artery crosses the second cuneiform bone and arches outwards over the bases of the metatarsal bones, beneath the long and short extensor tendons of the toes. It gives off the *second, third and fourth dorsal metatarsal arteries*, which run distally on the corresponding dorsal Interossei to the interdigital clefts, where each divides into two *dorsal digital arteries* for the sides of the adjoining toes. Each dorsal metatarsal artery gives off a *posterior perforating* branch which passes through the proximal part of the corresponding interosseous space to join the plantar arch; and at the distal parts of the spaces the dorsal and plantar metatarsal arteries anastomose through *anterior perforating* branches. The fourth dorsal metatarsal artery supplies a branch to the lateral side of the little toe.

The first dorsal metatarsal artery is the last branch given off the dorsalis pedis before it descends into the sole. It runs on the first dorsal interosseous muscle and divides at the interdigital cleft into two branches, one of which passes to the medial side of the big toe, while the other bifurcates to supply the adjacent sides of the first and second toes.

Variations

The more common forms of anomalous origins of the tibial and peroneal arteries were mentioned under variations of the popliteal artery. The perforating branch of the peroneal artery is invariably large if the anterior tibial artery is small, and then the former often provides the tarsal and arcuate arteries or may replace entirely the dorsal artery of the foot. Sometimes the peroneal and circumflex fibular arteries are branches of the anterior and not of the posterior tibial artery. The anterior tibial artery and its dorsalis pedis continuation may take the place, more or less completely, of the lateral plantar artery and the plantar arch: in that event the lateral plantar artery is small or absent, and occasionally the medial plantar artery is absent and replaced by branches of the lateral plantar or dorsalis pedis arteries.

Collateral Circulation

There are so many communications between the branches of the various arteries of the leg and foot that the effects of occlusion of one or even of two vessels on the circulation can be circumvented by the enlargement of alternative channels—unless the other vessels are diseased, or unless the block is at, or near, the bifurcation of the popliteal into the tibial arteries. As in the case of the palmar arches the arrest of haemorrhage from wounds of the plantar arteries or arch may prove a surgical problem if for any reason the vessels cannot be secured locally.

G A. G. M.

CHAPTER III

THE PHYSIOLOGY OF BLOOD FLOW IN THE LIMBS

SO much has been written about the human peripheral circulation that it has been difficult to select the material for this chapter. The aim has been to deal with certain aspects with which the author is fairly familiar rather than to review the whole subject. The nervous control of the vessels, the effects of sympathetic denervation, the action of the sympathomimetic hormones and the circulatory changes in exercise are topics which will be considered at some length. Others which will be mentioned more briefly are the relations between blood pressure and blood flow, the effects of temperature, the results of occlusion of the main vessels and the influence of the position of the limb. Obviously much relevant and valuable work is omitted and for this the reader is referred to Abramson's "Vascular Responses in the Extremities of Man in Health and Disease"[1] to the Ciba Foundation Symposium on "The Peripheral Circulation in Man"[2] as well as to the corresponding chapter in other texts on Peripheral Vascular Disease.[3, 4]

Arterial blood pressure and peripheral blood flow.—Over a century ago a physiologist set out to investigate the relation between the arterial blood pressure and the amount of blood flowing through an organ. He began with a glass tube and to quote Burton[5] "He discovered so much in purely physical *experiments*, that, as far as we know, he never achieved his goal of applying what he had found to the circulation." This man was Poiseuille and Poiseuille's Law is:

$$F = \frac{P. \pi r^4}{8\eta l}$$

where F is the flow in ml /sec.

P is the pressure difference between the ends of the tube in dynes/square cm.

r and l are the radius and length of the tube respectively in cm.

η is the coefficient of viscosity in poises

The term $\frac{\pi r^4}{8\eta l}$ is often referred to as R, the resistance to flow. About this resistance Sir William Bayliss[6] says "It is necessary to remember that the resistance opposed by a number of narrow channels is greater than that offered by a single large channel of sectional area equal to the sum of the smaller ones. This is stated correctly to be due to the friction in the latter case But the friction is not between the wall of the blood vessel and the blood but between the constituent elements of the liquid itself. The resistance of this internal friction was recognised by Newton and is an aspect of the mutual attraction of molecules which gives rise to the phenomenon of cohesion. . . In the case of liquids it causes the property known as viscosity.

Variations

The more common forms of anomalous origins of the tibial and peroneal arteries were mentioned under variations of the popliteal artery. The perforating branch of the peroneal artery is invariably large if the anterior tibial artery is small, and then the former often provides the tarsal and arcuate arteries or may replace entirely the dorsal artery of the foot. Sometimes the peroneal and circumflex fibular arteries are branches of the anterior and not of the posterior tibial artery. The anterior tibial artery and its dorsalis pedis continuation may take the place, more or less completely, of the lateral plantar artery and the plantar arch: in that event the lateral plantar artery is small or absent, and occasionally the medial plantar artery is absent and replaced by branches of the lateral plantar or dorsalis pedis arteries.

Collateral Circulation

There are so many communications between the branches of the various arteries of the leg and foot that the effects of occlusion of one or even of two vessels on the circulation can be circumvented by the enlargement of alternative channels—unless the other vessels are diseased, or unless the block is at, or near, the bifurcation of the popliteal into the tibial arteries. As in the case of the palmar arches the arrest of haemorrhage from wounds of the plantar arteries or arch may prove a surgical problem if for any reason the vessels cannot be secured locally.

G. A G M.

To refer again for a moment to Poiseuille's formula. The flow is proportional to the fourth power of the radius. Other things being equal tubes with radii in the ratio of 1 : 2 : 3 : 4 will have flows in the proportion of 1 : 16 : 81 : 256. The rates of the blood flow in the hand in the vaso-constricted and vasodilated states are about as 1 : 80. The transition from the slow to the rapid stream would therefore only require a threefold increase in the calibre of the vessels. However to achieve this the length of the smooth muscle

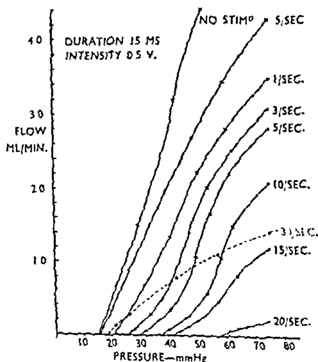


FIG. 46

Results showing "critical closing pressure."
curve
The

fibres would have to be trebled, a far greater change in length than that ever undergone by skeletal muscle fibres

Poiseuille's formula applies if (*a*) the flow is stream-line (laminar) (*b*) the fluid is simple and (*c*) the tubes are *indistensible*. As blood is not a simple fluid and blood vessels are *distensible* the Law only applies to the circulation within limits For further particulars the reader may consult the article in Medical Physics by Green[7] Apart from purely physical considerations there are biological ones.

to the stimulus of stretching by

a limb whose nerves were cut wa

by a rise of arterial pressure

We see then how the peripheral resistance in the vascular system is directly *proportional to the viscosity or internal friction of the blood*. Why is it then that the resistance is *greater in a number* of narrow channels, the arterioles, than in a smaller number of large channels, arteries, of equal sectional area, or even within limits of smaller cross sectional area?

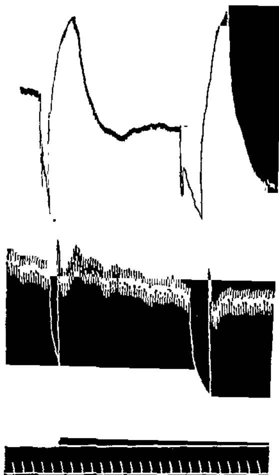


FIG 45

Results showing that stretching the wall of an artery may excite contraction.
Upper curve: volume of dog's hind leg, nerves cut
Lower curve: femoral arterial blood pressure
The abdominal aorta was compressed twice, for eight seconds. Each time collapse of the circulation was followed by marked vasodilatation in the legs after the blood was re-admitted Bayliss thought that this *vasodilatation was probably due to lack of* stimulation of the smooth muscle, due to the collapse of the vessels during the ischaemic period (*Bayliss.*[1])

" *When a liquid is flowing through* a tube the layer in contact with the wall of the tube is to all intents and purposes at rest, while that *in the centre* has the greatest velocity. Each layer is exposed to friction with the more rapidly moving layer next it; thus the velocity decreases progressively from the centre until the wall of the tube is reached, where friction holds the outermost layer at rest. Practically all the *friction is between the layers of the* liquid itself. Suppose that the tube is wide: the actual thickness of the peripheral layer, *in which the increase* of velocity from zero to its maximum takes place, only occupies a small part of the total space so that the greater part of the contents is moving at the same maximum rate *and experiencing* no perceptible internal friction Such is the case with the large arteries. In *the arterioles, on the other hand*, a much larger proportion of the cross section is occupied by liquid experiencing friction; the layer in which the velocity continues to increase may reach the middle of the tube *Thus the whole* volume of the blood in the arterioles may be exposed to friction, whereas only *a small fraction of it* is so exposed in the large arteries When the capillary area is reached the total width of the bed becomes somewhere about one thousand times that of the aorta, so that the rate of flow is very small The friction being nearly proportional to the velocity is accordingly very small in this region, as compared with *that in the arterioles*."

similar diversity of origin. Since . . . all the vasoconstrictors arise from the sympathethic and no other source, we should not expect to find any vasodilators of sympathetic origin."

TABLE I

VASOMOTOR INNERVATION OF BLOOD VESSELS

Bayliss's general concepts about the innervation of blood vessels compared with the views held today about the innervation of the blood vessels in the extremities of experimental animals and of man.

	BAYLISS *General concepts*	ANIMALS *Vessels of the limbs*	MAN *Vessels of the limbs*
1.	Each vessel has two kinds of nerves, vasoconstrictor and vasodilator.	Skin: vasoconstrictors only [illegible]	Skin of the hand: vaso- [illegible] Muscle vasoconstrictors and vasodilators
2	Vasoconstrictor fibres are sympathetic and leave the C N S. by the thoraco-lumbar outflow	Ditto.	Ditto.
3	Vasodilators are not sympathetic They are either parasympathetic or dorsal root fibres.	Skin no vasodilators. Muscle Centrally controlled vasodilators are sympathetic There are no others	Skin of the hand no vasodilators Skin of the forearm centrally controlled vasodilators are sympathetic. Muscle Centrally controlled vasodilators are sympathetic only. There are no others.
4	Principle of Reciprocal Innervation applies	Principle of Reciprocal Innervation does *not* apply.	?

3 Bayliss thought that central inhibition was mediated by vasodilators of two kinds, parasympathetic fibres and dorsal root fibres (antidromic vasodilators)

4 " The afferent fibres . . . obey a kind of reciprocal innervation, in that they excite the vasodilator centre and at the same time inhibit the tonic activity of the vasoconstrictor centre. Just as Sherrington showed that in reflex flexion of the knee, the centres for the flexors are excited, and those for the extensors inhibited The difference is that in the case of the smooth muscle of the arterioles, the effector muscle is one and the same . . " These four concepts are summarised in Table I

as would naturally be expected. But this distension was followed, on the return of blood pressure to the original level, by a contraction much beyond that which corresponded previously to the height of the blood pressure." This is shown in Figure 45. Bayliss thought that stretching had stimulated contraction of the arterial walls. The observation has recently been confirmed in both animals[8] and man.[9, 10, 11, 12] In animals the response is more marked in muscle vessels than in skin vessels and this may perhaps be because muscle vessels can adjust their blood flow more readily from one moment to another according to the needs of local tissue metabolism.[8]

Under the heading of arterial blood pressure and blood flow must be included some reference to the "critical closing pressure." In perfusion experiments in animals in which the pressure is lowered progressively it has been shown that the flow also decreases progressively for a while and then suddenly ceases although there is still a positive arterial pressure. The height of the mercury when this point is reached is the "critical closing pressure." This is shown in Figure 46. The physical explanation of this phenomenon is based on Laplace's Law which to quote Burton[5] "predicts that a small blood vessel must possess an intrinsic instability, such that if the pressure within it fell below a certain critical value (the "critical closing pressure") it would tend to close actively and completely. The critical closing pressure would increase with increasing tension in the wall (vasomotor tone) and with decreasing size of the vessel. *In understanding the critical closing pressure of small blood* vessels we have come to a new view of the nature of vascular spasm, namely that this means simply that the critical closing pressure is higher than the available blood pressure." Burton thought that critical closing pressure might also explain the opening and shutting of arterio-venous shunts.[5] The importance of critical closing pressures is for the future to decide.

The nervous control of the blood vessels in experimental animals.—It is well known that vascular tone can be increased or in some cases decreased by nervous excitation. Pavlov[13] showed that the adductor muscle of the mussel can be made to contract by stimulating one set of nerves, and to relax by stimulating another set. He concluded that there must be two distinct ways in which the nerve fibres terminate in order that one may excite and the other inhibit. The concepts of the nervous control of the peripheral circulation laid down in most physiological textbooks are those formulated by Bayliss and summarised in his classic monograph "The Vasomotor System"[6] Of these concepts the following may be recalled in Bayliss' own words:—

1. "As a general rule, in fact, we find that smooth muscle or any other muscle not subject to voluntary control such as that of the heart is supplied with nerves of two kinds, excitatory and inhibitory . . . It is naturally to be expected that the vascular muscles do not form an exception to this rule."

2. "We notice further that . . . the two kinds of nerve fibres arise from different regions of the central nervous system. Wherever we have definite knowledge of the two kinds of fibre supplied (to the blood vessels) we find a

imilar diversity of origin. Since . . . all the vasoconstrictors arise from the sympathethic and no other source, we should not expect to find any vasodilators of sympathetic origin."

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VASOMOTOR INNERVATION OF BLOOD VESSELS

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The thirty years since Bayliss wrote the monograph have seen many notable advances in the physiology of the nervous control of the circulation. The work of Folkow, Uvnäs and others in Scandinavia on experimental animals has been outstanding. According to the Scandinavian school Bayliss' original concepts would now need to be modified as follows:—

1. Nearly all organs are supplied by centrally controlled vasoconstrictor fibres, but few tissues, neither the intestines[14, 15] for example, nor the skin [16, 17] receive centrally controlled vasodilator fibres.

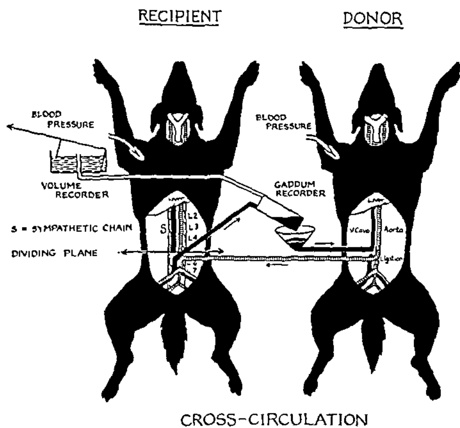


FIG. 47

Diagram showing procedure used to investigate the influence of the baroceptors upon the blood vessels in the dog's hind limb

(*After Folkow Strom and Uvnäs* 21)

2 Vasoconstrictor and vasodilator fibres do arise from the same part of the nervous system. The thoraco-lumbar sympathetic outflow contains both the vasoconstrictor fibres and the vasodilator fibres to the skeletal muscles[16, 18] and to the muscles of the tongue.[19]

3. The dorsal root fibres are not under central nervous control.

4. In the case of nervous regulation of the blood vessels the principle of "reciprocal innervation" does not appear to apply For example—

(i) the reflex regulation by the baroceptors of the vascular beds in the intestines, skeletal muscles and skin is mediated solely by modification of the vasoconstrictor tone.[15, 20, 21]

(ii) so is the regulation of the blood vessels in the skin by the temperature regulating centre.[22, 23]

(iii) on the other hand the vasodilatation induced in the skeletal muscles by excitation of special areas of the cortex or hypothalamus is mediated entirely by sympathetic vasodilator fibres [24]

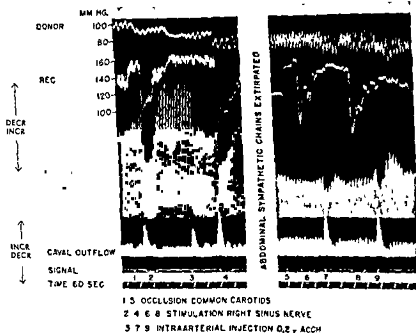


Fig. 48

These conclusions, based on animal experiments, are summarised in Table 1 One or two of these experiments may be mentioned to enable the reader to judge for himself the importance of these results However the soundness of the technique, the thoroughness of the controls, the number and consistency of the results and above all the discussion of them in relation to the results previously obtained by Bayliss and others cannot be fully appreciated without reference to the original papers which are fortunately in English.

We may first consider the influence of the pressure receptors upon the vascular bed in the dog's hind limb One of the procedures used to investigate this may be seen in Figure 47 The hind limbs of one dog (the recipient) were perfused from the circulation of another dog (the donor). This was done to

avoid the possibility of alterations in the circulation in the lower part of the recipient's body due to alterations of the blood pressure or of the hormone concentration in the upper part of this animal. The rate of the blood flow in both of the recipient's hind limbs was recorded in the inferior vena cava. The rate of the cutaneous blood flow was recorded in a saphenous vein.

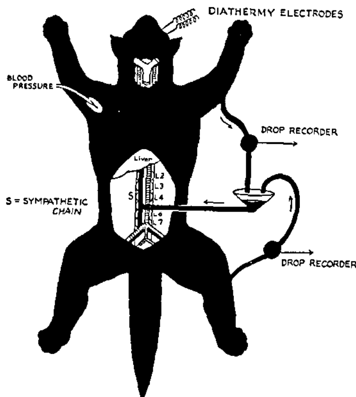


FIG 49
Diagram showing procedure used to investigate the effect of warming the temperature regulating centre on cutaneous circulation of the limbs
(*After Folkow, Strom and Uvnas*[23])

Reduction of the blood pressure in the carotid sinus of the recipient following occlusion of the common carotid arteries (Fig. 48, 1) caused reflex *vasoconstriction in the legs. Stimulation of the carotid sinus nerve* (Fig. 48, 2 and 4) caused vasodilatation in both caval and saphenous areas.

To see if the abdominal sympathetics were implicated both sympathetic chains were now removed. Neither occlusion of the common carotids (Fig. 48, 5) nor stimulation of the sinus nerve (Fig. 48, 6 and 8) had any effect whatsoever. Intra-arterial injection of acetyl choline (Fig. 48, 7 and 9) caused vasodilatation and showed that the vessels could have dilated. Stimulation of the dorsal root fibres (not shown in Fig. 47) caused vasodilatation in the skin and showed that these fibres could have mediated vasodilator impulses. Folkow, Strom and Uvnas[21] concluded that the pressor receptor reflexes must be mediated by sympathetic fibres alone and that the fibres in the dorsal roots played no part.

In other experiments with the sympathetic outflow intact, the action of the vasoconstrictor fibres was blocked with dibenamine After dibenamine lowering the pressure in the carotid sinuses by clamping the carotids no longer caused vasoconstriction in the hindlegs. Although the vasodilator fibres

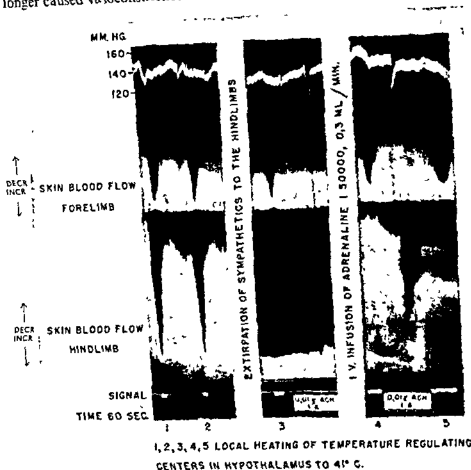


FIG. 50
Results showing that sympathectomy abolishes the action of the temperature regulating centre on the cutaneous circulation in the limbs. (*After Folkow, Strom and Uvnas* [23])

remained intact there was no sign of reciprocal innervation. On the other hand atropine, which totally blocks the dilator fibres, had no influence on the vasomotor effects evoked from the carotid sinus receptors. The reflexes from the carotid sinuses were carried out solely by modification of the vasoconstrictor tone [20]

The experiments done by the Scandinavian workers on the effect of the temperature regulating centre are also most instructive.[22, 23] One of the procedures is seen in Fig. 49 Diathermy electrodes were inserted into the

anterior part of the hypothalamus. The cat was eviscerated to expose the abdominal sympathetic chain. The rate of the blood flow was recorded in the cephalic vein of the forelimb and also in the saphenous vein of the leg. The blood in these veins comes mainly from the skin. Local heating of the temperature regulating centre by the diathermy (Fig. 50, 1 and 2) caused marked vasodilatation in the skin of the legs. To see if the abdominal chain was implicated the sympathetic chain was now removed. Heating the centre (Fig. 50, 3) caused vasodilatation in the forelegs as before but it now had no effect whatsoever on the circulation in the hindleg. Neither however did an intra-arterial injection of acetyl choline (Fig. 50); owing to the loss of sympathetic tone the vessels were already almost maximally dilated. Vasoconstrictor tone was re-established by a continuous intravenous infusion of adrenaline Even so heating the centre (Fig 50, 4 and 5) had no effect on the circulation in the hindleg Intra-arterial injection of acetyl choline now caused vasodilatation (Fig. 50) showing that the vessels of the hindleg *could have dilated* Stimulation of the dorsal root fibres (not shown in Fig. 50) caused vasodilation in the skin; the dorsal root fibres could have mediated vasodilator impulses. Folkow, Strom and Uvnas[22, 23] concluded that the central effects of temperature regulation must be mediated by sympathetic fibres only, the fibres in the dorsal roots played no part.

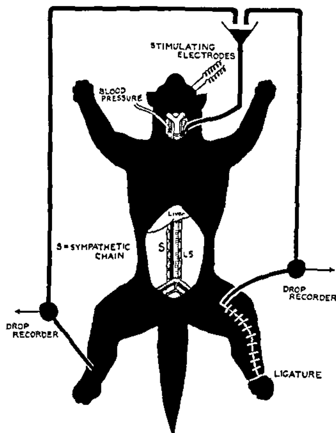


FIG. 51

Diagram to show procedure used to investigate the effect of stimulation of a part of the hypothalamus on the blood flow in the skin and skeletal muscles of the cat's hind limbs

(After Eliasson Folkow, Lindgren and Uvnäs [24])

In further experiments the action of the vasoconstrictor fibres was blocked with dibenamine. After dibenamine, stimulation of the sympathetic nerve supply to the skin had no effect and they concluded there are no vasodilator fibres to skin.[16, 17] The cutaneous vasodilatation caused by heating the hypothalamus must be due solely to release of vasoconstrictor tone.

The last example is taken from the recent work on the sympathetic vasodilator supply to the skeletal muscles. One of the procedures used is seen

in Figure 51. The cat was adrenalectomised to avoid errors due to adrenaline secretion Stimulating electrodes were inserted into the appropriate part of

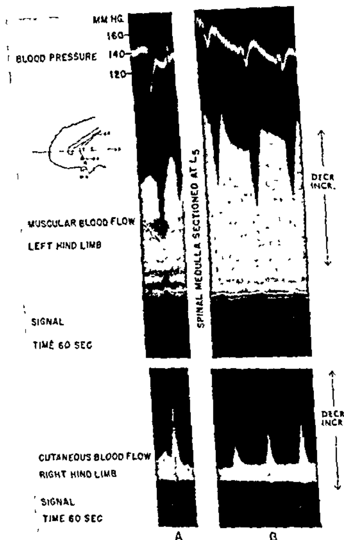


FIG. 52

Results showing that stimulation of a part of the hypothalamus caused vasodilatation in the skeletal muscles, and vasoconstriction of the skin of the hind limb These responses were mediated by sympathetic fibres, since they persisted after section of the spinal cord below the sympathetic outflow to the legs

(After Eliasson, Folkow, Lindgren and Uvnäs 24)

the hypothalamus The rate of the blood flow was measured in the left femoral vein This blood came from the skeletal muscles only, as a ligature had been tied round the leg above the ankle and a sheet of cellophane had

anterior part of the hypothalamus. The cat was eviscerated to expose the abdominal *sympathetic chain*. The rate of the blood flow was recorded in the cephalic vein of the forelimb and also in the saphenous vein of the leg. The blood in these veins comes mainly from the skin. Local heating of the temperature regulating centre by the *diathermy (Fig. 50, 1 and 2)* caused marked vasodilatation in the skin of the legs. To see if the abdominal chain was implicated the sympathetic chain was now removed. Heating the centre (Fig. 50, 3) caused vasodilatation in the forelegs as before but *it now had no effect* whatsoever on the circulation in the hindleg. Neither however did an intra-arterial injection of acetyl choline (Fig. 50); *owing to the loss of sympathetic tone* the vessels were already almost maximally dilated. Vasoconstrictor tone was re-established by a continuous intravenous *infusion of adrenaline* Even so heating the centre (Fig. 50, 4 and 5) had no effect on the circulation in the hindleg. Intra-arterial injection of *acetyl choline now caused* vasodilatation (Fig. 50) showing that the vessels of the hindleg could have dilated Stimulation of the dorsal root fibres (not shown in *Fig. 50) caused* vasodilation in the skin; the dorsal root fibres could have mediated vasodilator impulses. Folkow, Strom and Uvnas[22, 23] concluded that the central effects of temperature regulation must be mediated by sympathetic fibres only. the fibres in the dorsal roots played no part.

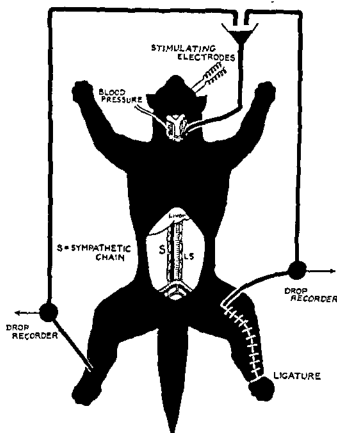


Fig 51

Diagram to show procedure used to investigate the effect of stimulation of a part of the hypothalamus on the blood flow in the skin and skeletal muscles of the cat's hind limbs

(After Eliasson, Folkow, Lindgren and Uvnas 24)

In further experiments the action of the vasoconstrictor fibres was blocked with dibenamine. After dibenamine, stimulation of the sympathetic nerve supply to the skin had no effect and they concluded there are no vasodilator *fibres to skin.*[16, 17] *The cutaneous vasodilatation* caused by heating the hypothalamus must be due solely to release of vasoconstrictor tone.

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pathetic vasoconstrictor nerve supply as well as the somatic sensory and motor fibres Figure 53 is from one of Gilding's experiments.

Nervous control of limb blood vessels in man.—Armed with the foregoing notions about the nervous control of the blood vessels in the limbs of experimental animals we can now examine that of the circulation in the human extremities. It will be convenient to consider first the evidence for the existence of vasoconstrictor and vasodilator fibres to the different tissues of the arm and leg and then the use of these fibres by the vaso-motor centre.

Skin of the fingers and hands.—It is generally agreed that this is plentifully supplied with vasoconstrictor fibres. The marked hyperaemia that follows the blocking or cutting of the sympathetic supply to the hand can only be due to the interruption of vasoconstrictor nerve impulses.

The existence of vasodilator fibres seems unlikely. Only a summary of the evidence can be given. Lewis and Pickering[3] observed that the vasodilatation induced by body warming in the fingers of Raynaud patients could be delayed by ulnar nerve block. Interruption of vasodilator nerve impulses was considered to be the explanation. Arnott and Macfie[7] measured the rate of heat loss from the fingers of both hands by calorimetry. The ulnar nerve on one side was blocked and the body warmed to induce maximum vasodilatation in the little finger of the opposite side Heat loss from the two little fingers remained equal They concluded that there were no vasodilator fibres; if there had been heat loss would have been greater from the normally innervated digit.

P Gaskell[28] recorded the rate of the blood flow through both hands plethysmographically during vasodilatation induced by body warming. Neither blocking the radial, median and ulnar nerves, nor the intra-arterial infusion of atropine had any effect on the blood flow through the vasodilated hand Gaskell concluded that cholinergic vasodilator nerves were *not* implicated.

Skin of the forearm.—According to Grant and Holling[29] only a small rise in the temperature of the forearm skin follows cutaneous nerve block. This is believed to signify a meagre supply of vasoconstrictor fibres.

Unlike the hand the forearm appears to be supplied with cutaneous vasodilator fibres The evidence is as follows. Blocking one of the cutaneous nerves of the forearm causes a *reduction* of skin temperature in *indirectly* heated subjects.[29] This cannot be due to the cessation of sweating which would tend to make the skin *warmer* The alternative is a decrease in blood flow caused by the interruption of impulses in vasodilator fibres. From this may be inferred that there may be a vasodilator nerve supply to the skin of the rest of the body, with the exception of that of the hands and feet.

been wrapped round the limb between the muscles and the skin. The rate of cutaneous blood flow was recorded in the saphenous vein in the right leg. Stimulation of the hypothalamus caused vasodilatation in the muscles but vasoconstriction in the skin (Fig. 52A). As there was a fall in blood pressure the vasodilatation in the muscles could not have been a reflex from the baroceptors. It might have been due to muscular contractions but these could not be seen. To eliminate this possibility the cord was cut leaving intact the sympathetic nerve supply. Hypothalamic stimulation still caused muscular vasodilatation (Fig. 52B) Atropine was given to paralyse the sympathetic vasodilator fibres. Hypothalamic stimulation no longer caused vasodilatation in the muscles. Therefore the vasodilator fibres must be solely responsible



FIG. 53

Experiment showing that sympathetic vasoconstrictor fibres to the skin of the cat's paw travel in the mixed nerves. Left ulnar nerve cut Left stellate ganglion stimulated throughout the experiment Brom-phenol blue rapidly injected into the internal saphenous vein One minute later cat rapidly killed by exsanguination

Skin in area of ulnar nerve distribution deeply stained Section of the nerve had prevented vasoconstriction because it had divided most if not all of the sympathetic vasoconstrictor fibres to that area

(Gilding [25])

As stimulation of this region of the hypothalamus also often caused vasoconstriction in the skin and intestines, tachycardia, constriction of the spleen and dilatation of the pupil, Eliasson, Folkow, Lindgren and Uvnäs[24] thought that the activation of the vasodilator fibres must be part of the reaction pattern of emergency states in which a sudden increase of muscle blood flow is often needed for muscular activity.

In connection with the peripheral pathway of the sympathetic fibres we may recall the beautiful work of Gilding.[25] After cutting the ulnar nerve in one of the forelimbs of the cat he stimulated the stellate ganglion on the same side continuously so as to excite and maintain strong vasoconstrictor tone in all the tissues to which its fibres were distributed. A dye was then injected intravenously. About a minute later the cat was killed and the colour of the skin and muscles of the forelimb was inspected The structures supplied by the ulnar nerves were much darker in colour than any others. Cutting the ulnar nerve must have prevented vasoconstriction in the area of its distribution. This must have been because it contained the sym-

to the same extent when the body is warm the total increase in blood flow through them would be about $1\frac{1}{2}$ litres per minute

The skeletal muscles in man probably have a vasodilator nerve supply. This was shown as follows.[33, 34] During posthaemorrhagic fainting the arterial

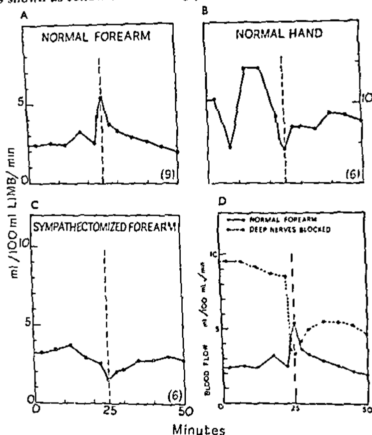


FIG. 55

blood pressure falls precipitously but the forearm blood flow increases (Fig. 55A) The increase is in the muscles and not in the skin since it does not occur in the hand which is mostly skin (Fig. 55B). The increase in the forearm blood flow is of nervous origin since it is absent after sympathectomy (Fig.

Skeletal muscle.—The existence of vasoconstrictor fibres has been shown as follows.[30, 31, 32] The rate of the blood flow in the two forearms is normally equal (Fig. 54A). Radial, median, and ulnar nerve blocks in one arm double the rate of the forearm blood flow (Fig. 54B). This is due to paralysis of sympathetic nerve fibres since the response is unobtainable in sympathecto-

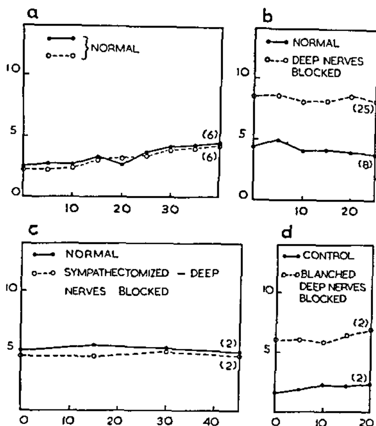


FIG. 54

Results showing that the sympathetic nervous system maintains vasoconstrictor tone in the blood vessels of the skeletal muscles of the resting forearm

a, equal blood flow in right and left forearms
b, *blood flow doubled after radial, median and ulnar nerve block on left forearm*
c, equal blood flow after radial, median and ulnar nerve block in sympathectomised left forearm
d, blood flow doubled after radial, median and ulnar nerve block in left forearm Skin blanched by adrenaline electrophoresis

(*After Barcroft, Bonnar Edholm and Effron* [30])

mised subjects (Fig. 54C) The response can be obtained after blanching the forearm skin by adrenaline iontophoresis and it is therefore deep to the skin most probably in the skeletal muscles (Fig. 54D). It is probably due to blocking vasoconstrictor nerve impulses in sympathetic fibres to skeletal muscle blood vessels. About 1/100th of the skeletal muscular system is enclosed in the forearm plethysmograph and if the other muscles vasodilate

scarcely alter the blood flow in the extremity. It might make a large difference to the circulation in the bone itself.

It will be remembered that Bayliss thought that all blood vessels would have both vasoconstrictor and vasodilator nerves, and it is of interest to recall that the vessels in the skeletal muscles and probably those in the skin of the arms and legs conform to this precept. An exception has to be made in the case of the specialised skin of the fingers and hand (and in the case of that of the toes and feet?) which is innervated by vasoconstrictor fibres only. See Table I.

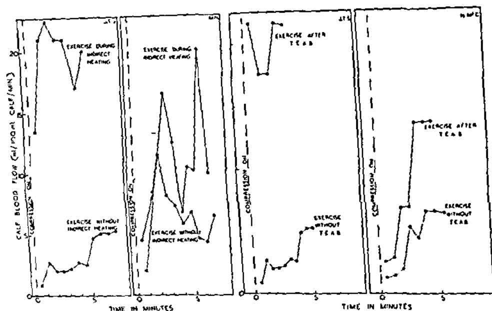


FIG. 56

Results showing that the sympathetic maintains vasoconstrictor tone in the collateral vessels of the hip which can be released by indirect heating and by TEAB.

After occlusion of the femoral artery and severe exercise of the calf muscles, the blood flow through the calf is ... ound the hip In these circumstar ... and by indirect heating must ha ... aused by

Central nervous control of vessels in the hands and feet.—The blood flow in the specialised vessels in these parts is almost entirely determined by the intensity of the central vasoconstrictor tone. In a comfortable warm environment the average blood flow in the hands is between 4 and 9 ml./100 ml. hand/min according to the results of different investigators.[42] Marked fluctuations take place from moment to moment. Burton[43,44] has shown that these occur simultaneously in all the digits. Sympathectomy abolishes these alterations in blood flow which are due to changes in the activity of the vasomotor centre.[46] Apart from these irregularities in the behaviour of the vasomotor centre, which cannot be explained, the centre is influenced to a

55c). It is greater in normal forearms than in forearms whose nerves have been blocked. This is probably because vasodilator nerve impulses cannot reach the skeletal muscle vessels in the nerve block forearms (Fig. 55D).

Arteries.—Very little is known about the sympathetic innervation of the large arteries in man. The femoral artery of the cat is not innervated by the sympathetic, neither is that of the rabbit Kinmonth, Simeone and Perlow exposed this vessel in the groins of these animals and made frequent measurements of its diameter with a dissecting microscope and micrometer eyepiece during various procedures. Stimulation of the sympathetic chain just below the diaphragm caused erection of the hairs on the tail and shrinkage of the paw but had no effect on the diameter of the femoral artery.[35] Further work is needed on the sympathetic innervation of the arteries in man.

Veins.—Lewis and Landis[36] found that human veins were supplied with sympathetic vasoconstrictor fibres. Their observations were made on two subjects two to three weeks after unilateral sympathectomy. Both forearms were congested to a pressure of 40 mm. Hg. by cuffs on the upper arms. The veins on the sympathectomised side stood out much more prominently although the pressure of the blood distending them could not have been any greater than that distending the normally innervated veins on the opposite side They concluded that normal veins are subject to sympathetic vasoconstrictor tone.

Collateral vessels.—Sympathetic vasoconstrictor fibres supply the collateral vessels around the hip,[37] the lower part of the thigh, the knee and the elbow[38] and no doubt those elsewhere. Some experiments on the hip collaterals will serve to illustrate how proof has been obtained of the sympathetic innervation of such vessels.[37] The rate of the blood flow through the calf of the leg was measured plethysmographically in normal subjects after severe exercise on the calf muscles performed during occlusion of the femoral artery In such circumstances, the peripheral resistance in the calf being very low, the rate of the blood flow in the calf depends upon the resistance in the collateral vessels near the hip. To see if the sympathetic maintained tone in these collaterals the collateral flow was measured by the method which has just been described both before and after procedures likely to release such tone The results were then compared To release vasoconstrictor tone either the body was warmed or tetra-ethyl ammonium bromide was injected intravenously. Figure 56 shows that both these procedures increased the collateral blood flow, the inference being that the collaterals of the hip are normally supplied by sympathetic vasoconstrictor fibres and possess vasoconstrictor tone

Bone.—Sympathetic vasoconstrictor fibres have been demonstrated in the dog[39] but not yet in man. Bone blood flow is so very small[40, 41] that the release of any sympathetic vasoconstrictor tone in the bone vessels would

constriction excited by the low temperature.[30] In spite of the release of vasoconstrictor tone in the hand and feet the arterial blood pressure is scarcely altered because a compensatory vasoconstriction occurs in the splanchnic area.[31] In other words there is a localisation of function in the vasomotor centre according to the different tissues of the body.

TABLE II

NUMBER OF ANASTOMOSES PER 1 CM.² SURFACE AREA

Hand	Index finger	
	Nail-bed	501
	Tip	236
	Palm, 3rd phalanx	150
	" 2nd "	20
	" 1st "	93
	Palm	
	Metacarpo-phalangeal joint, 3rd finger	31
	Thenar eminence	113
	Hypothenar eminence	96
Foot	*Second toe*	
	Nail bed	593
	Pad	293
	Sole, near heel	197

A short digression will be made here on the subject of arterio-venous anastomoses. It is probable that the pronounced actions of the vasomotor centre on the circulation in the hands and feet, just described, take place in these vessels The arterio-venous anastomoses in the hand and feet are far larger than any that have yet been found in other parts of the limb and this may explain why the effect of the vasomotor centre on the circulation is most pronounced distally.

The discovery of these large arterio-venous anastomoses was made by anatomists towards the end of the last century. The first physiological study of their action in man was made by Grant and Bland[32] and is of great interest. Lewis had told Grant and Bland that when vasodilatation takes place in the hand the rise in the sk[illegible] ...curred to Grant and Bland that [illegible] place in arterio-venous anastor[illegible] region. As little was known about the distribution of these vessels in the skin of different parts of the limbs this was studied first The arterio-venous anastomoses were found to measure 20-70 μ in diameter, and were situated at about the same depth as the sweat glands, far too deeply to be visible from the surface. Figure 57 sh[illegible] microphotograph of an arterio-veno[illegible] per square [illegible] The number [illegible] ble II. In the

marked extent by psychic and sensory stimulation. Mental arithmetic, apprehension, the feeling of ice on the skin or of a distended bladder and so on all excite strong vasoconstriction. For this reason precautions have to be taken during experiments on the hand blood flow to see that the subject is comfortable and relaxed, and that the results are interpreted correctly. The vasoconstriction that occurs in the hand after taking a deep breath is probably another example of the effect of sensory stimulation, in this instance due to discharge from stretch receptors in the chest.[47] Sympathectomy abolishes all these psychic and sensory responses.



FIG. 57
Section of the pad of the human toe, showing arterio-venous anastomoses (A, B) lying deeply in the neighbourhood of the sweat glands (× 25)
(*Grant and Bland* [52])

The activity of the vasomotor centre is decreased to some extent during sleep[49] and possibly too towards the end of pregnancy [49] In these circumstances the hand and feet are warm and the blood flow above the normal.

The circulation in the hand and feet plays an important part in the regulation of heat loss from the body In an uncomfortably warm environment central vasoconstrictor tone is released and the rate of blood flow increases to between 20 and 40 ml./100 ml hand per minute. The release of tone, in the hands at any rate, is complete in really warm subjects for blocking the radial, median and ulnar nerves is not followed by any further hyperaemia.[28] On the other hand the release of tone may be delayed or absent altogether in cold feet. In this case although tone is released centrally in the normal manner, the effect is not manifested peripherally owing to the vaso-

constriction excited by the low temperature.[30] In spite of the release of vasoconstrictor tone in the hand and feet the arterial blood pressure is scarcely altered because a compensatory vasoconstriction occurs in the splanchnic area.[31] In other words there is a localisation of function in the vasomotor centre according to the different tissues of the body.

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	„ 1st „	93
	Palm	
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	Thenar eminence	223
	Hypothenar eminence	96
Foot	Second toe	
	Nail bed	593
	Pad	293
	Sole, near heel	597

A short digression will be made here on the subject of arterio-venous anastomoses. It is probable that the pronounced actions of the vasomotor centre on the circulation in the hands and feet, just described, take place in these vessels. The arterio-venous anastomoses in the hand and feet are far larger than any that have yet been found in other parts of the limb and this may explain why the effect of the vasomotor centre on the circulation is most pronounced distally.

The discovery of these large arterio-venous anastomoses was made by anatomists towards the end of the last century. The first physiological study of their action in man was made by Grant and Bland[32] and is of great interest. Lewis had told Grant and Bland that when vasodilatation takes place in the hand the rise in the skin temperature begins in the fingertips. It occurred to Grant and Bland that this might be because the vasodilatation takes place in arterio-venous anastomoses in this region. As little was known about the distribution of these vessels in the skin of different parts of the limbs this was studied first. The arterio-venous anastomoses were found to measure 20-70 μ in diameter, and were situated at about the same depth as the sweat glands, far too deeply to be visible from the surface. Figure 57 shows a microphotograph of an arterio-venous anastomosis in the pad of the human toe. The number per square cm. of skin surface of different localities is shown in Table II. In the

hand the greatest number was found in the nail-bed and thence in descending order of number in the tip of the finger, the palmar surface of the phalanx, the thenar eminence, the hypothenar eminence, the palmar surface of the first phalanx, and the palmar surface of the second phalanx. There were no AV anastomoses in the dorsum of the fingers and toes, or in the flexor surface of the lower part of the forearm or calf, or in the lower part of the ear. Other areas proximal to the hand and feet were not studied

Grant and Bland then investigated the function of these vessels. Did the arterio-venous anastomoses participate in the vasodilatation in the hand induced by local cooling (see page 147)? To test this the time interval between the beginning of cooling and the first rise in the temperature was measured in different localities and the results were compared with the number of anastomoses The temperature of the skin of the finger-tip rose sooner than the temperature of the palmar surface of the middle phalanx. The number of arterio-venous anastomoses per sq. cm. was 236 in the first instance and twenty in the second. The temperature of the skin of the thenar and hypothenar eminence rose sooner and much higher than did the temperature of the flexor surface of the forearm. The skin of the former contained about 100 anastomoses per sq. cm., there were none in the forearm skin. In other words the greater the number of arterio-venous anastomoses the sooner and the higher did the temperature rise. They concluded that the arterio-venous anastomoses were the vessel chiefly responsible for cold vasodilatation. (An exception had to be made in the case of the lobe of the ear which dilated promptly and vigorously but did not contain any anastomoses, or at any rate none anything like as large as those in the fingers and palm). Grant and Bland did not carry out similar experiments to see if the anastomoses were chiefly responsible for the vasodilatation caused by the loss of sympathetic tone during body warming. Very likely they are, for in this case too the earliest rise in temperature occurs in the finger tips Very likely the anastomoses are the site of the spontaneous fluctuations in the hand blood flow and of the vasoconstriction caused by psychic or sensory stimulation.

Central nervous control of the vessels in the forearm and calf.—The vascular responses to central nervous control recorded by the forearm plethysmograph are far less obvious than those just described in the hand Fluctuations are not so conspicuous and mental disturbance causes vaso-dilatation in these parts [53, 54] When the body is warmed the forearm blood flow increases several fold This response is absent after sympathectomy.[55]

The results obtained with the forearm plethysmograph are the sum of the blood flows in the skin, muscle and other tissues which the instrument encloses. According to Abramson the proportions are skin and subcutaneous tissue 13 per cent.; skeletal muscle 58 per cent. and bone plus fat and tendon 28 per cent [53] The separation of small vascular changes which occur in the forearm skin from those which take place in the muscles is technically difficult. Two methods may be mentioned. The skin calorimeter, and forearm

plethysmography combined with adrenaline iontophoresis. Hensel's skin calorimeter measures the rise in temperature of water flowing over a small area of skin, the result is a function of the rate of the cutaneous blood flow and is independent of the rate of the circulation in the deeper tissues.[56] In the plethysmographic method the blood flow in both forearms is measured with plethysmographs after the skin circulation in one has been suppressed by adrenaline introduced by electrophoresis.[57, 58] The difference in the results obtained for the two sides is the rate of the skin blood flow and the result obtained in the electrophoresed forearm is the rate of the blood flow through the skeletal muscles. Figure 58 shows the relation between the blood flow in the normal forearm and that recorded simultaneously in skeletal muscles of the contralateral iontophoresed forearm in a number of normal subjects.[58] Very roughly one-quarter goes through the skin and three-quarters through muscle when the subject is comfortably warm.

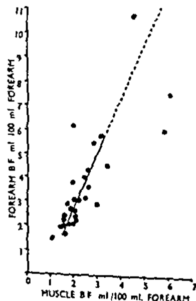


Fig. 58

Blood flow through the muscles of the forearm (skin blanched by adrenaline iontophoresis) *plotted* against total forearm blood flow recorded simultaneously in the contralateral normal forearm

(After Cooper Edholm and Mottram 58)

The following facts about the central nervous control of the circulation in the forearm skin and in the skeletal muscles has been obtained by these and other methods.

The circulation in the forearm skin behaves like that in the hand, that is to say it fluctuates synchronously with the fluctuations elsewhere in the skin and it is constricted by psychic and sensory stimuli. The effects are of course very small as compared to the total forearm blood flow. The increase in the forearm blood flow during body warming is mainly in the skin and represents a *very large* increase in the cutaneous blood flow.[39, 40] How much of this is due to the release of vasoconstrictor tone and how much to active vasodilatation[39] is *not* known. Sympathectomy abolishes these responses.

The circulation in the skeletal muscle of the forearm also fluctuates spontaneously[38] but the arterioles dilate *rather* than constrict after psychic stimuli.[33] As already mentioned muscle vessels are subject to sympathetic vasoconstrictor tone[30] and muscle blood flow decreases slightly during indirect heating.[39] Why the circulation in muscle should be affected by temperature regulation is not known. The *vasodilatation* in the skeletal muscles that takes place in fainting and is of central origin has already been mentioned. The decrease in the resistance of the muscle blood vessels during fainting appears to be greater than that elsewhere in the body and to be mainly responsible

for the fall in blood pressure and so for the loss of consciousness.[31] Alterations of posture also affect the forearm blood flow, probably because of the effect on the circulation in the skeletal muscles. This will be referred to later. The rôle of the sympathetic supply to the skeletal muscle vessels will also be deferred for the present.

Origin of vasomotor fibres to human limbs.—Sympathectomy abolishes all known central nervous regulation of the circulation in the limbs. It will be recalled that Bayliss thought that the vasoconstrictor and vasodilator fibres would leave the CNS in different regions but that the Scandinavian School had found that the vasoconstrictor and vasodilator fibres to the limb of experimental animals are both of sympathetic origin. This is true of man too. There is no evidence in man of any central nervous control of the limb vessels by dorsal root or parasympathetic fibres. These facts have been summarised in Table I.

Reciprocal innervation.—Bayliss believed in the action of reciprocal innervation in vascular responses (Table I). However the Scandinavian School were unable to confirm this; according to them changes in the circulation in the skin and skeletal muscles from the temperature regulating centre and carotid sinuses were mediated entirely by adjustment of the vasoconstrictor tone. It is not known if reciprocal innervation acts in man. It was believed to do so in fainting but this was before the Scandinavian work was published and the results could be explained just as well by active vasodilatation alone

The local effect of temperature.—This was investigated in the hand by Spealman.[61] Blood flow was measured with the plethysmograph. Each experiment lasted for three hours and was done with the water in the plethysmograph at a constant temperature between 2 and 35 °C. The results of five records of the blood flow taken during the last hour were averaged The experiments were repeated in uncomfortably hot, normal, and uncomfortably cold environmental temperatures so as to obtain information on the interaction of the local and body temperatures on the hand blood flow Table III shows the averaged results for all subjects For any given local temperature the hand blood flow was a function of the environmental temperature. For example when the hand was in water at 15°C the blood flow in the cold, normal and warm environments were 0 3, 0 9 and 5·5 ml per 100 ml hand respectively. This is explained by the decrease in vasoconstrictor tone with increase in the environmental temperature. For any given environmental temperature Table III shows that the local temperature has a pronounced effect on the hand circulation At 15°C the rate of the circulation is less than it is when the water is either warmer or colder. The explanation of the greater flow at higher temperatures is not fully understood and involves the direct action of heat on the smooth muscle coat of the vessels as well as the indirect action of heat on the production of vasodilator metabolites (See Freeman)[62] It is interesting to learn that the ox's isolated carotid artery constricts when

it is warmed.[63] If temperature has the same effect on human arteries then its action on those in the hand must be overcome by some concomitant vasodilator action possibly that of increase in the concentration of tissue metabolites When the chronically denervated forearm is warmed to 35°C. and above the blood flow increases much more than it does in the normal limb. The explanation is not known.[64]

TABLE III

THE EFFECT OF LOCAL TEMPERATURE (WATERBATH) AND ENVIRONMENTAL TEMPERATURE ON THE RATE OF THE BLOOD-FLOW IN THE HAND

Twelve readings of the blood-flow were made on each subject during the third hour of the experiment and the results were averaged.

Temperature of the hand (waterbath)	*Hand blood-flow, ml. per 100 ml. hand per minute*		
	Subjects (3) uncomfortably warm 32°C. D.B.; 28°C. W.B	Subjects (6) comfortable 24°C. D.B.; 19°C. W.B	Subjects (3) uncomfortably cold 16°C. D.B.; 13°C. W.B
35	20·6	5·9	1·9
25	—	2·7	0·6
20	8·1	1·3	—
15	5·5	0·9	0·3
10	—	2·5	1·9
5	6·8	4·3	—
2	6·4	—	—

Table III also shows that there was an increase in the rate of the circulation in the hand when it was cooled below 15°C. This is the so called "cold vasodilatation." It was first described by Lewis[65] who noticed that the immersion of fingers in water below 15 - 18°C. caused vasoconstriction soon followed by vasodilatation In general the lower the temperature the more decided the reaction. If the fingers were kept in the cold water periods of vasoconstriction and vasodilatation alternated, the so-called "hunting reaction." Cold vasodilatation occurred after section and degeneration of the sympathetic nerve supply to the fingers, and also for a short while after section of the somatic nerve. However as it was unobtainable after degeneration of these nerves Lewis thought it was caused by an axon reflex. He believed that this was excited by [illegible] Later Greenfield and his colleagues [illegible] ...ans of the calorimeter[67-71] As in certain circumstances they were able to obtain the vasodilatation in chronically denervated fingers[72] and in normal fingers during the

action of local anaesthetics[73] they concluded that it was not fundamentally dependent upon nervous action. It was true that it was much larger in innervated fingers. As it occurred in fully atropinised fingers acetyl choline

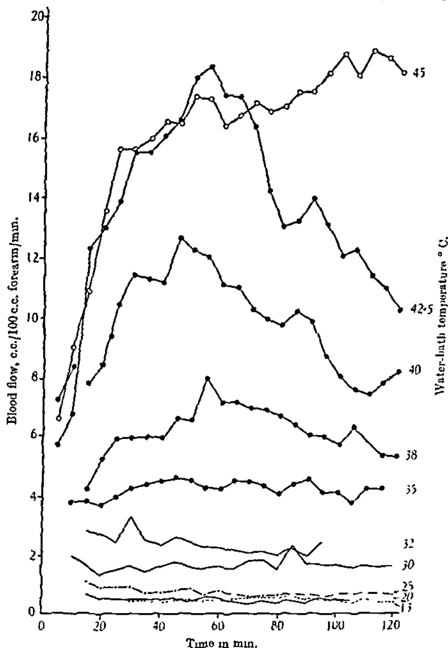


FIG. 59

Results showing the effect of temperature on the blood flow in the forearm The arm was placed in the waterbath at time 0. Blood flows were recorded for two hours at a chosen constant waterbath temperature Averaged results obtained in five subjects. (*Barcroft and Edholm*.[76])

was probably not implicated[74] It is interesting to note the effect of extremes of heat and cold on the blood flow in the paw of the cat. These cause marked vasodilatation in the sympathectomised paw but only slight vasodilatation in

the totally denervated paw. Furthermore antihistaminics have no effect on the vasodilatation in the paw with intact sensory innervation but they abolish the slight vasodilatation in the totally denervated paw. These results and others show that the marked vasodilatation in the paw with the somatic innervation intact is due to an axon reflex mediated by the small pain fibres. The slight vasodilatation in the denervated paw is due to the action of histamine liberated by the damaged cells, and closely resembles Lewis' "red reaction."[75]

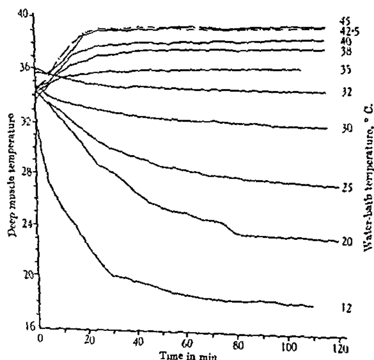


FIG. 60

temperature ... at a chosen constant waterbath temperature Averaged results obtained in five subjects.
(Barcroft and Edholm 76)

The effect of local temperature on the circulation in the forearm[76, 77] and foot[78] has been investigated using the plethysmograph. The blood flow in the forearm was measured every five minutes for two hours at a number of constant plethysmograph temperatures ranging from 13 to 45°C. Figure 59 shows the results The rate of flow ranged from 0 5 ml./100 ml. forearm per minute at 13°C. to 17·6 ml at 45°C. The results can be divided into three categories:—

(*a*) 13 - 35°C. Slight decrease in flow, taking place in the first quarter hour.

(*b*) 37 - 42°C. Flow increasing to a maximum in the first hour and then decreasing. The so called " die away."

(*c*) 45°C. Flow increasing for the first half to threequarters and then remaining constant. The effects of temperature on the blood flow in the foot were similar.[78]

Immersion of the forearm in water at 18°C. caused no discomfort or change in body temperature probably because the venous return was almost nil; the flow was so slow that if forearm veins had been cut the blood would have emerged in drops at intervals of several seconds. Lefevre[79] thought that the effect of local temperature only penetrated a short distance under the skin. Figure 60 shows that in fact it penetrates the whole thickness of the forearm; after two hours in water at 13°C. the temperature of the forearm muscles near the head of the radius was only about 18°C., about the temperature of frog's muscle. It was still possible to write legibly. The results are in accordance with the marked decrease in cardiac output caused by cooling the whole body.[80] The explanation of the " die away " in the 37 - 42°C. range is not known. Its absence at 45°C. may be because of slight damage to the skin which remained red for a long time after being in such hot water.

Reactive hyperaemia.—When the circulation to a limb is restored after it has been arrested for a short time the skin flushes. This is reactive hyperaemia, and it involves the underlying tissues also. Lewis and Grant[81] studied reactive hyperaemia in the forearm with the plethysmograph and showed that " it is evidently related in its degree to one factor namely the blood flow debt which is usually a product of the amount by which the flow is reduced and the time over which the reduction has been maintained " They thought that it was caused by the accumulation of a histamine-like vasodilator substance in the tissues during the period of arrest. Although it is generally accepted that a vasodilator metabolite is mainly responsible it is not likely that histamine itself plays an important part Some authors claim that the histamine concentration is increased in venous blood collected during the hyperaemic period[82] but others deny it.[83] Reactive hyperaemia appears to be almost un-influenced by the previous administration of anti-histamine substances[84, 85] It is now known that the extra amount of blood which traverses the tissues after release of the circulation is not necessarily closely related to the blood debt.[10, 86-88 and more recently 89] Moreover part of the hyperaemia is probably of mechanical origin, due to the lack of stretching of the arterial walls during the period of arrest and so to a falling off in the stimulus for contraction If the forearm is " packed " with blood just before arresting the circulation the arteries empty less completely and the ensuing hyperaemia is subnormal.[90] Unfortunately our knowledge of the fundamental causes of reactive hyperaemia is still very far from complete. Yet it is an important mechanism. For

example whenever the body rests, parts of it are brought under pressure, where it makes contact with its support. This results in diminution in arterial inflow and eventually discomfort is produced. As a result the position is moved so that there is now a change in the area of pressure and the parts previous made ischaemic are immediately flooded by blood and restored to their normal state again.[1]

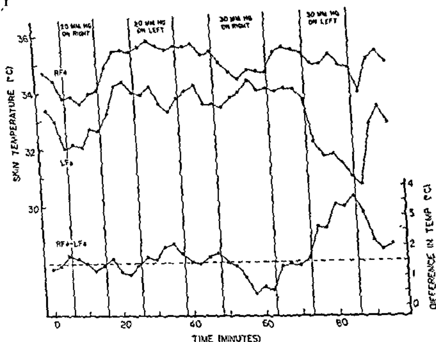


FIG 61

Results *showing* that venous compression decreases the amount of blood flowing through *the skin of the* fingers

Top curve: temperature of *the skin* of the fourth finger of the right *hand*. *Middle curve*, temperature *of the skin of* the fourth finger of the left hand. *Bottom curve*: shows how much colder or *hotter* the temperature of the ... of the fourth finger of the ...

The difference between the ... an air pressure on one or ot... was further raised to 30 mr... of the finger of the corresp... due to venous compr...

Effect of slight venous compression.—It will be convenient to discuss this before considering the question of posture and limb position, and it is of course relevant to the action of tight bandages and so forth. Figure 61 is from an experiment by Halperin, Friedland and Wilkins[10] and shows that venous compression decreases the rate of the circulation in the hand. The subject was covered with blankets to induce mild vasodilatation in the hands. The temperature of the fourth finger of both hands was recorded thermoelectrically. Venous pressure in the fingers could be increased by increasing

(*a*) 13 - 35°C. Slight decrease in flow, taking place in the first quarter hour.

(*b*) 37 - 42°C. Flow increasing to a maximum in the first hour and then decreasing. The so called " die away."

(*c*) 45°C. Flow increasing for the first half to threequarters and then remaining constant. The effects of temperature on the blood flow in the foot were similar.[78]

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It has been suggested that venous ligation should be done because the distension of the vessels will greatly improve the exchange of substances between the blood and tissues. This was tested as follows. Immediately after the beginning of compression the subject commenced flexion and extension of the foot once a second; this he continued for about a minute until forced to stop by intolerable discomfort. Now followed a short period of freedom from pain. But as the veins distended and the skin got cyanosed pain began again and soon became intolerable (Fig 62D). The experiment strongly suggests

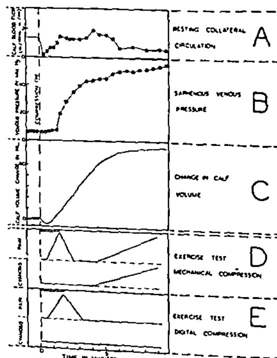


Fig 62
Results showing that the circulation in the leg and the exchange of substances between the blood and the tissues of the leg are better when the femoral artery alone is occluded than they are following the occlusion of both the femoral artery and vein. For explanation see text (*Shepherd.*[95])

that the exchange of substances between th[illegible]
down rather than speeded up by [illegible]
further experiment in which the [illegible]
of the vein being avoided; [illegible] compressed digitally, compression
exercise in this experiment was not followed by pain or cyanosis (Fig. 62E)

Effect of limb position.—In a recumbent subject raising the limb above 15° from the horizontal progressively decreases the rate of the circulation through the toe[96]. The effect of lowering the limb to the dependent position

the air pressure in the plethysmographs in which the hands were enclosed. The two upper curves show the temperature of the fingers of the right and left hands. The bottom curve shows the finger temperature difference, that is to say, how much hotter or colder the right finger was than the left. The figure shows that increasing the venous pressure to 20 mm. Hg. in one or other of the hands had very little effect on the finger temperature difference. On the other hand increasing the venous pressure to 30 mm. Hg. caused the finger of the congested hand to become distinctly cooler than that on the control side This must have been due to decreased blood flow. Similar results were obtained on six subjects, and were confirmed by other well controlled experiments in which the effect of raised venous pressure on the circulation was studied with the plethysmograph or by the method of arterio-venous oxygen differences.

Effect of slight venous congestion.—Although small degrees of venous congestion reduce the rate of the blood flow through the fingers[91] they do not appear to do so in the forearm.[92] This difference may be due to a difference in the behaviour of the muscle blood vessels. Apparently the increase in the peripheral resistance caused by the venous congestion is to some extent offset by a compensatory vasodilatation in the skeletal muscles.[93, 94]

The effect of occlusion of the main vessels on the limb circulation.—When the main artery of a limb has to be ligatured there is a difference of opinion as to whether it is better for the nutrition of the limb to tie the main vein or not Some experiments on the effect of arterial and venous occlusion on limb blood flow are relevant.[95] A mechanical compressor was used to compress one or both main vessels of the leg near the groin The compressor was an arm hinged to a table having at the other end a rubber pad which could be centred over the vessels. When in use a 9·5 kg. weight was placed on the arm over the pad. The rate of the circulation in the calf was measured with the plethysmograph. Figure 62A shows the effect of occlusion of both femoral artery and vein. Calf blood flow decreased to about a sixth of its resting rate and then increased reaching the resting rate again in one-half to six minutes. After this it decreased progressively once more till the end of the tenth minute when compression was stopped. We are now concerned with the explanation of this final decrease in the calf blood flow While it was taking place the volume of the calf was increasing (Fig. 62C). And this coincided with visible distension of the veins and with rising venous pressure (Fig 62B); the pressure in the long saphenous veins rose to 50 mm Hg Was the decrease in flow real or was it only apparent due to failure of the plethysmograph to record the real blood flow in the distended veins? It was almost certainly a genuine decrease for reactive hyperaemia followed the release of the circulation signifying a preceding state of circulatory insufficiency (reactive hyperaemia did not occur if the circulation was released before the beginning of the final decrease in calf blood flow). This experiment showed that ligature of the main artery of a limb will restrict the blood less than ligature of both the artery and vein

It has been suggested that venous ligation should be done because the distension of the vessels will greatly improve the exchange of substances between the blood and tissues. This was tested as follows. Immediately after the beginning of compression the subject commenced flexion and extension of the foot once a second; this he continued for about a minute until forced to stop by intolerable discomfort. Now followed a short *period of freedom from* pain. But as the veins distended and the skin got cyanosed pain began again and soon became intolerable (Fig. 62D). The experiment strongly suggests

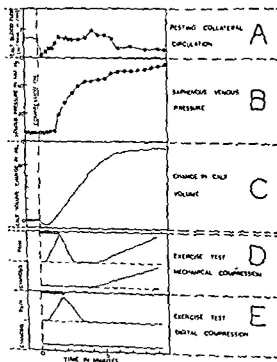


FIG 62

Results showing that the circulation in the leg and the exchange of substances between the blood and the tissues of the leg are better when the femoral artery alone is occluded than they are following the occlusion of both the femoral artery and vein. For explanation see text. (*Shepherd.*[illegible])

that the exchange of [illegible]
down rather than [illegible]
further experiment [illegible]
of the vein being [illegible]
pain or cyanosis (F[illegible]). [illegible] followed by

Effect of limb position.—In a recumbent subject raising the limb above 15° from the horizontal progressively decreases the rate of the circulation through the toe[96]. The effect of *lowering* the limb to the dependent position

is not clear. Decrease in flow through the toes has been reported[96] as has increase in flow through the leg,[97] arm[98] and fingertips.[99]

The effect of body posture.—When the posture of the whole body is altered the action of the heart and circulation is modified so as to maintain an adequate blood flow to the brain. This is done reflexly by the baroceptors in the carotid sinuses and aortic arch. The baroceptors have a marked effect in man. Figure 63 shows the rise in arterial blood pressure and in pulse rate after blocking both carotid sinus nerves with local anaesthetic in a conscious subject.[100]

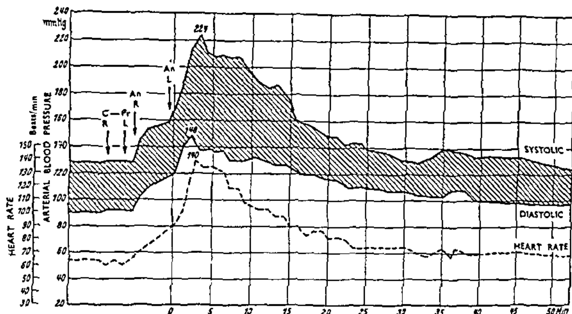


FIG. 63
Results showing the effect of bilateral carotid sinus nerve block on the arterial blood pressure and heart rate in man
C—Pr, pressure over the carotid sinus, An, carotid sinus nerve block; R, right, L, left
(*Klinische Wochenschrift*)

When a supine subject stands up his systolic pressure falls 5 - 40 mm. Hg. The effect of this on the baroceptors is to cause reflex vasoconstriction which restores the pressure to normal within half a minute.[101] The extent to which the vessels in the hand and feet are implicated in this response does not appear to have been investigated plethysmographically. When subjects were tilted 75° from the horizontal there was a drop in skin temperature, most marked in the legs, but also seen in the hands, abdomen, chest, neck and forehead.[102] This is shown in Figure 64, and suggests that vasoconstriction takes place in the hands and feet. Figure 65 shows that the blood vessels in the forearm, most probably those in the skeletal muscles, are also implicated. This response is abolished by sympathectomy.[103, 166]

It is worth noting that the circulation time is increased in the erect position probably owing to increase in the volume of venous blood in the leg.[104]

It seems then that the condition most favourable to the blood flow through the arm and leg may prevail when the subject is lying down with the limb dependent. In these circumstances vasoconstriction induced by the baroceptors will be minimal and the resistance to flow will be reduced by hydrostatic stretching of the vessel walls

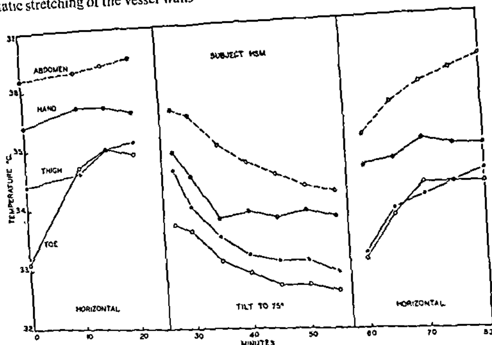


Fig. 64

Results showing the effect of gravity on the circulation in the skin
When the subject was tilted into the upright ... ature of th... d vaso-

Sustained muscular contraction.—Gaskell[105, 106] discovered that two factors tend to alter the blood flow in contracting muscle. The accumulation of vasodilator metabolites tends to increase the rate of flow, and mechanical compression of the vessels tends to decrease it. This was the result of experiments on the dog and frog

In man the circulatory changes in the gastrocnemius soleus muscle during sustained contraction have been recorded by means of a thermojunction inserted deeply in the calf of the leg[107] The limb was immersed to the knee in either hot or cold water to establish a temperature difference between the muscle and the blood entering it Four strengths of contraction were used 0 5, 0 1, 0 2 or 0 3 maximal. To perform one of the three weaker contractions the subject sat on a bicycle saddle beside the water... in which his leg was imme... pressure with the ba... suitably weighted lever.

To perform the strongest contraction he stood on tiptoe on the leg in the bath with the knee straight.

Figure 66 shows the results obtained during the weakest contraction. The curves on the left show that the temperature of the muscle during the exercise approached that of the entering blood, that is to say warm muscle cooled and

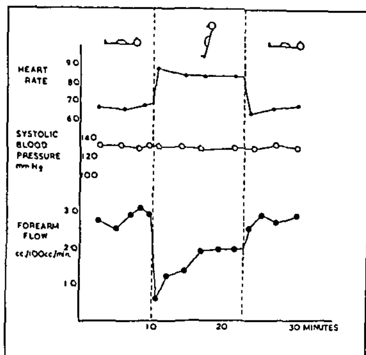


FIG. 65

Results showing the effect of the baroceptors in the carotid sinuses on the blood flow in the forearm
When the body is tilted into the erect position the arterial blood pressure falls, inhibition of the vasomotor centre diminishes and sympathetic vasoconstrictor tone increases in the blood vessels of the forearm

(*Brigden, Howarth and Sharpey-Schafer* [103])

cold muscle became warmer. The result could have been caused by hyperaemia. To confirm this the exercises were repeated after the circulation had been arrested in the thigh. The results are seen on the right hand side of Figure 66. Now, as would be expected, the temperature changes previously attributed to hyperaemia were absent. Another inference may be made. When the circulation was free the exercise was terminated after half an hour and no discomfort was felt. But when it was done during circulatory arrest intolerable pain in the calf made it impossible to continue longer than quarter of an hour. This difference must have been due to the functional significance of the circulation. The results obtained during the 0·1 maximal contractions were similar.

The situation during the performance of the two strongest contractions was altogether different as may be seen in Figure 67. Both the warm and the cold muscle got warmer during this exercise. There was no sign at all of the converging temperature changes indicative of hyperaemia. We see from

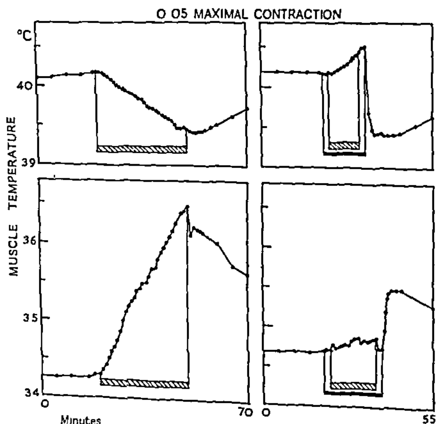


FIG. 66

Results ... an gastrocnemius soleus

Upper e

the curves on the right hand side of Figure 67 that when the exercise was done during circulatory arrest the temperature changes were so similar to those recorded while the circulation was free as to suggest strongly that there was no circulation in either case. Moreover ...

... through the muscle

in either case. Similar results were obtained during the experiments in which the subject stood on tiptoe, the strongest contraction.

The following conclusions seem justified. Weak sustained contractions are accompanied by hyperaemia. Vasodilatation overcomes the effect of

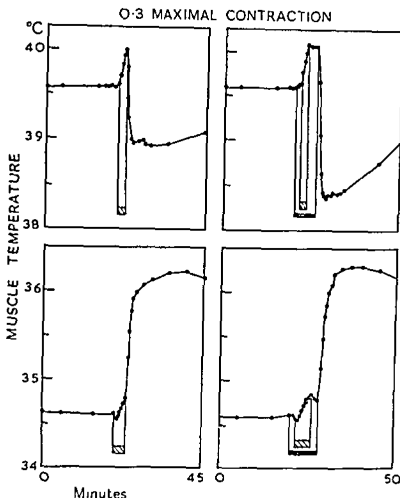


FIG. 67

Results showing that strong sustained contraction of the human gastrocnemius soleus muscle is ischaemic.
Upper curve: waterbath temperature 42°C, "hot" muscle
Lower curve: waterbath temperature 32°C; "cold" muscle
Hatched rectangle: 0 5 maximal contraction.
Solid rectangle. circulation arrested in thigh
During exercise the temperature of both "hot" and "cold" muscle increased with the circulation free and when it was arrested There could not have been any appreciable blood flow through the muscle in either case

(*After Barcroft and Millen* 107)

mechanical compression of the vessels This is probably the situation in the blood vessels in the muscles of catatonic subjects Above a certain rather critical strength of contraction the picture changes and mechanical compression takes precedence. This is not surprising considering the enormous pull on the tendon. For example in the experiment shown in Figure 67 the pull on the

Achilles tendon was equivalent to about three times the body weight! In spite of such great tension the intramuscular pressure may not exceed the diastolic blood pressure[108, 109, 110] and it may well be that nipping or kinking of the artery at a particular point is what brings the circulation almost or quite to a standstill.

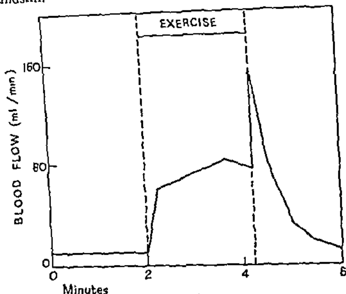


FIG 68

Results showing the effect of rhythmic exercise on the blood flow through the dog's gastrocnemius muscle

(*After Kramer, Obal and Quensel 112*)

Rhythmic muscular contraction.—Chauveau, Professor of veterinary physiology at Lyons and his assistant Kaufmann[111] made one of the earliest and most striking observations of the effect of rhythmic exercise on muscle blood flow in animals. They noted that bleeding from the horse's labial vein became much more profuse while the animal ate hay. Experiments on the isolated gastrocnemius muscle of the dog show that strong rhythmic contractions are accompanied by hyperaemia. This is seen in Figure 68. The maximum flow occurs immediately after the end of the exercise. The explanation is that the blood flow is checked mechanically by each contraction and it can only attain its maximum after contractions cease.[112] The behaviour of the circulation during and after strong rhythmic exercise of human calf muscles is similar[113] (Fig. 69). This implies that in walking and running the blood must go through the calf muscles in spurts.

Cause and mechanism of the vasodilatation in muscle during exercise.—Experiments on animals on the effect of curare show that the vasodilatation is due to some physico-chemical change initiated by the contractile process.[114, 115] Curare does not interfere with the liberation of substances at motor or sympathetic nerve endings nor with their action on blood vessels. Yet it abolishes

in either case. Similar results were obtained during the experiments in which the subject stood on tiptoe, the strongest contraction.

The following conclusions seem justified. Weak sustained contractions are accompanied by hyperaemia. Vasodilatation overcomes the effect of

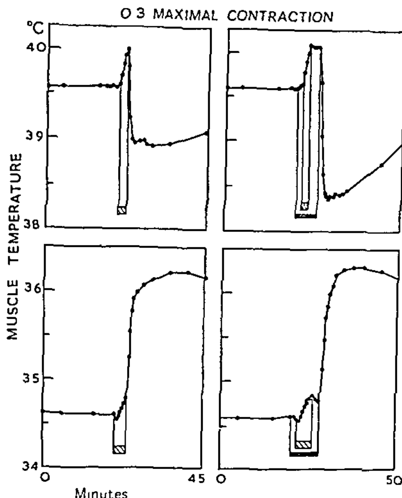


Fig. 67

Results showing that strong sustained contraction of the human gastrocnemius soleus muscle is ischaemic
Upper curve: waterbath temperature 42°C; "hot" muscle.
Lower curve: waterbath temperature 32°C; "cold" muscle
Hatched rectangle: 0 5 maximal contraction.
Solid rectangle: circulation arrested in thigh.
During exercise the temperature of both "hot" and "cold" muscle increased with the circulation free and when it was arrested There could not have been any appreciable blood flow through the muscle in either case
(*After Barcroft and Millen* 107)

mechanical compression of the vessels This is probably the situation in the blood vessels in the muscles of catatonic subjects Above a certain rather critical strength of contraction the picture changes and mechanical compression takes precedence. This is not surprising considering the enormous pull on the tendon. For example in the experiment shown in Figure 67 the pull on the

iodo-acetic acid.[120] More recently Gollwitzer-Meier[121] has shown that the changes in pH of the venous blood from a muscle during and subsequently to activity bear no relationship to the associated hyperaemia.

It is not likely that histamine plays an important part, because the post-contraction hyperaemia was unaffected by mepyramine.[115] Acetyl choline cannot be completely excluded for Fleisch[124] has shown that it is a potent stimulator of the axon reflex which dilates the femoral artery. Other substances that have already been considered but remain to be critically examined are ATP[120, 121] and potassium ions.[122] Granting the existence of some physico-chemical or chemical change which induces the vasodilatation there remains the question of whether this acts directly on the muscle blood vessels or through the medium of a local axon reflex. The many-fold increase in muscle blood flow during activity implies a reduction of the resistance to flow to a very small fraction of its resting value. This must occur in the arterioles since these are the site of most of the resistance to flow. The arterioles could be penetrated by vasodilator substances. The effectiveness of dental anaesthesia is a good example of the remarkable ease with which chemical substances can penetrate living tissue by diffusion. Hilton has suggested another explanation. In the dog muscular activity causes dilatation of the femoral artery. This is mediated by an axon reflex from the active muscles.[124, 125] It is suggested that during exercise a similar reflex dilates the arterial tree in the muscle itself. This receives some support from the fact that powerful contractions of the cat's leg muscle are no longer accompanied by hyperaemia if the muscle has been previously treated with substances likely to block the action of a local axon reflex.[115]

Few experiments in man have been done on the cause and mechanism of the vasodilatation. Grant[126] showed that when exercise is performed during circulatory arrest the vasodilatation takes place after the blood flow is restored (see Figs. 66 and 67). In these circumstances it cannot be due to cortical excitation of either sympathetic or motor nerve fibres or to acetyl choline which is very rapidly destroyed in the tissues. It must be caused by a physico-chemical change in the muscle persisting till the blood is restored. Both histamine[127] and adenosine triphosphate[128] introduced directly into the brachial artery cause marked vasodilatation in the forearm muscles but whether they do so in exercise is not known. Histamine is probably not implicated in man since reactive hyper[illegible] drugs.[85] Durin[illegible] the oxygen sat[illegible] For this reason it is unlikely th[illegible] anoxic drive plays a significant part in causing this hyperaemia.[129]

Th[illegible] exer[illegible] [illegible]sible for [illegible] to what [illegible] Cannon's emergency

both the hyperaemia and the contractions excited by motor nerve stimulation. Direct stimulation of the curarised muscle causes both hyperaemia and contractions. This shows that hyperaemia is due to a local physico-chemical change initiated by the contractile process.

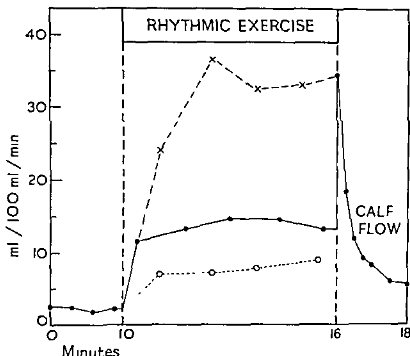


FIG 69

Results showing the behaviour of the blood flow in the human

ation Rapid flow
ained contraction
nd Dornhorst.[113])

The nature of this process has intrigued physiologists since Gaskell's original suggestion of " metabolites " The present state of our information from the results of animal work has been summarised by Hilton[115] as follows " O_2 lack can be excluded; for Krogh[116] showed that tissue oxygen pressure does not fall, but in fact rises, in active muscle The changes in hydrogen ion concentration that occur physiologically were shown by Fleisch[117] to be too small to account for the increase in blood flow through the active tissues, while Krogh[118] quotes evidence showing that a CO_2 tension which will produce an acidity far higher than that ever occurring normally has an insignificant effect on vessels, especially the arteries of the frog's tongue. Lactic acid, injected into muscle arterially has very little vasodilator effect*,[119] and the post contraction hyperaemia is unaffected when lactic acid formation is prevented by

* Nevertheless the buffering action of tissue fluid may not be as good as that of blood and it is possible that the release of lactic acid directly into the tissue fluid surrounding the blood vessels might cause marked vasodilatation

Taking all the available facts into consideration it is unlikely that the sympathetic nervous system plays much part in opening the blood vessels in human skeletal muscles at the beginning of exercise.

The pumping action of the muscles on the veins.—This has been shown in several ways[134 137]. Figure 71 shows the marked fall in venous pressure on the dorsum of the foot which takes place when an upright subject raises and lowers his heels. This is due to emptying of the veins in the calf by the muscle pump. Its action has also been demonstrated plethysmographically in the recumbent subject as seen in Figure 72. During each 10 sec. period of rhythmic flexion and extension of the foot decrease in calf volume occurred as the blood in the veins was pumped out. Increase in calf volume took place at the beginning of each 10 sec. rest period as the veins refilled from below. The pump has considerable power. As Figure 72 shows it can overcome a venous pressure of 90 mm. Hg.

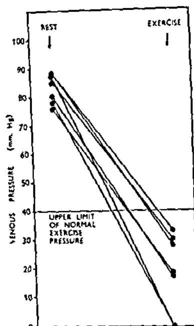


FIG. 71

Results showing the effect of exercise on the venous pressure in the foot. Each line shows the change in pressure for one subject. During the exercise the subject marked time smartly, each foot being raised nine inches sixty times per minute.

(*Walker and Longland* 137)

The action of the sympathomimetic amines.—The effects of adrenaline and noradrenaline on the circulation in the limb are frequently referred to in connection with exercise, emotional stress, Raynaud's disease and supersensitivity after sympathectomy and it will be convenient to describe these effects now.

The influence of the two amines in the circulation in the hand has been studied with the plethysmograph during infusions made into the brachial artery[138]. The apparatus is shown in Figure 73. Saline was infused continuously throughout the experiments and one or other of the amines was added to the saline from time to time to study its effect on the vessels. Both amines cause vasoconstriction in the hand[138].

The entry of adrenaline into the general circulation has a more complicated effect on the hand blood flow and has been studied by means of intravenous infusions.[139] Besides the strong local action which decreases the blood flow there is a weak inhibitory action on the vasomotor centre which tends to increase it. As long as the adrenaline is present in the general circulation the local constrictor action predominates. However after the infusion is stopped the local effect wears off first and constriction gives place to an after-dilatation. This subsides as the central inhibitory effect disappears,

theory would lead one to suppose that it would play at least some part. The idea is supported by the fact that stimulation of the motor area of the cerebral cortex causes vasodilation in the limbs which is brought about by nerves[130] and because stimulation of the hypothalamus causes vasodilatation in the skeletal muscles which is mediated by sympathetic vasodilator fibres.[24] These facts have been established in experimental animals.

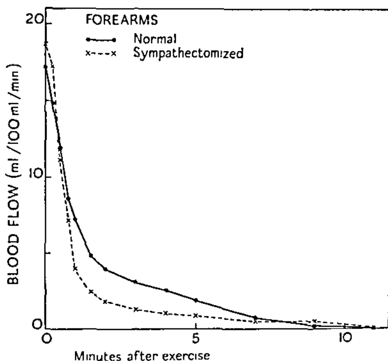


FIG. 70
Results showing normal vasodilatation in sympathectomised muscle after exercise (*After Grant.*[126])

Grant[126] found that the hyperaemia in the forearm following a few minutes of exercise of the forearm muscles is the same in extent and duration in sympathectomised and in normally ennervated limbs Further if the sympathetic nerve supply was of functional use in exercise then surely some restriction of a subject's capacity for bicycling and for other activities would be expected after sympathectomy. But lessening of the faculty for the performance of muscular work is never even thought of as a contraindication to the operation. Shepherd[131] has shown that sympathectomy has no effect on the functional performance of the calf muscles of arteriosclerotic patients. Pickering and Hess[30] showed that changes in sympathetic tone occur simultaneously in the hand and feet and by analogy one would expect the change in sympathetic tone in skeletal muscles in exercise should be manifested simultaneously throughout the whole skeletal musculature of the body In this connection Ruosteenoja[132] found that there was only a very small increase in the blood flow in the resting forearm during the first five minutes of hard pedalling on a stationary bicycle.

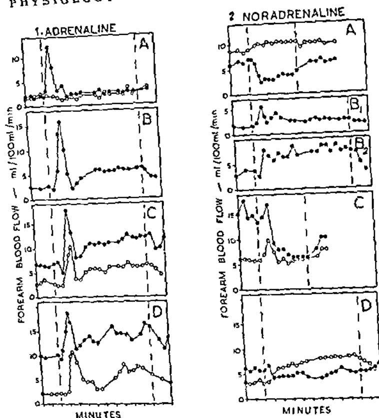


FIG. 74

Left: the effect of intravascular inf...

1A ...
of ...
in ...

... intravenous infusion Transient and sustained ...
acutely sympathectomised (d...
(circles) Results in a...

Right: the effect of intravasc...
flo...

2A. intrabrachial infusion (dots) Constriction No change in the oppo...
forearm ...

2B₁, B₂, intravenous infus...
2C, intravenous infusion ...
No change in the opposit...
the direct vasoconstricto...
dilatation, with the resu...

2D intravenous infusion vasoconstriction in the sympathectomised forearm (dots) and vasodilatation in the opposite normal forearm (circles) Results in accordance with those obtained in C (*Whelan*.[345])

and is absent in sympathectomised subjects. *This is probably the explanation* of the facial flush seen after stopping intravenous adrenaline infusions.

The actions of adrenaline and noradrenaline on the circulations in the forearm and calf have been studied by several authors[140-144] whose conclusions

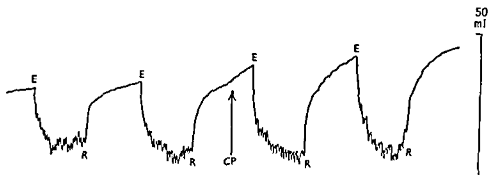


FIG. 72

Results showing shrinkage in calf volume during rhythmic exercise due to the action of the "muscle pump."
Plethysmographic record of the volume of the calf of the leg Shrinkage denoted by downward movement of the writing point
E, pedal pressed down once a second for ten seconds R, rest for ten seconds
CP, cuff just above the knee inflated to 90 mm Hg until end of recording
(Barcroft and Dornhorst 1949)

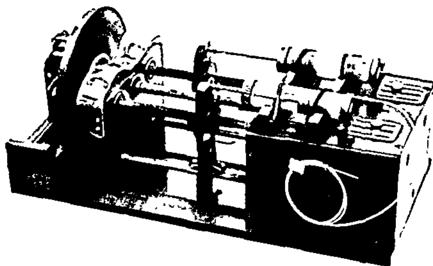


FIG. 73

Photograph of infusion apparatus made by P T Machell in the Radiotherapy Workshop, St Thomas's Hospital, London. (*Duff*.[178])

have been reviewed by Whelan.[145] Figure 74, 1A shows the direct effect of an intra-arterial infusion of adrenaline on the forearm circulation. There is an initial transient vasodilatation lasting for about a minute after which the circulation returns to the pre-infusion level for the remainder of the infusion

rise in blood pressure or to direct action on the vasomotor centre there will be a release of vasoconstrictor tone which will tend to increase muscle blood flow. However this vasodilator action of noradrenaline, such as it is, will be more or less counteracted by its local constrictor effect on the muscle blood vessels

Chemical transmitters at vasomotor nerve endings in human skin and muscle.—The Scandinavian physiologists have shown that the vasoconstrictor nerves to the skin of the dog and cat liberate noradrenaline[147, 148] and that acetyl choline is liberated by the vasodilator fibres in the skeletal muscles.[149]

The identity of the transmitters in man is not known. No doubt the vasoconstrictors to the skin are adrenergic but it is uncertain whether the substance liberated is noradrenaline or adrenaline.

Noradrenaline seems the more likely to be the transmitter at the vasoconstrictor nerve-endings in human skeletal muscle. Introduced into the brachial artery in small doses it causes prompt constriction of the muscle vessels as would be expected if it were the transmitter (*see* Fig. 74, 2A). On the other hand adrenaline causes an initial vasodilatation (Fig. 74, 1A) and a very large dose is required to constrict the vessels subsequently However adrenaline liberated at nerve endings in intimate contact with the smooth muscle cells of the vessels might have a purely vasoconstrictor action and the possibility that it is the transmitter cannot be excluded

Acetyl choline dilates human muscle vessels,[147] as would be expected if the vasodilator nerves were cholinergic. However atropine does not abolish the fall in blood pressure in fainting[150] and further experiments are needed before acetyl choline can be accepted as being the transmitter substance.

Sympathetic denervation.—Twenty years ago Telford[151] wrote these words "It is an everyday observation that the brightly injected and warm limb which follows at once on sympathectomy begins to lose its heat and colour in a few days We should learn much if we could truly interpret this change." We will now be concerned with these and other results of dividing the sympathetic fibres to the limbs.

In the same year that Adson and Brown[152] reported that lumber sympathectomy caused a permanent rise of 12°C. in the temperature of the toes Lewis and Landis[36] stated that the tone of the capillaries had returned by the second day after operation and that the tone of the digital arteries had returned by the fourth day. To obtain more [illegible] the hand[153] foot[154, 155] [illegible] measured daily befo[illegible] sympathectomy. Figure 75 shows the averaged results obtained on the hand and foot, subdivided into two groups according to whether the arteries were normal or diseased Sympathectomy increased the blood flow in normal hands about six times. This hyperaemia subsided quickly. on the sixth day the hand flow was only double the pre-operative rate and the difference was still less on the fourteenth day. On the

period. The cause of the transient dilatation is not known. It takes place in the skeletal muscles and we may infer from its very existence that the local action of adrenaline on the muscle blood vessels is really a very complex affair. If during an intra-arterial infusion the concentration of adrenaline is increased stepwise each increase in concentration is immediately followed by a fresh transient dilatation. Infusions of very high concentrations of adrenaline, outside the physiological range, cause little or no transient dilatation followed by sustained vasoconstriction till the end of the infusion. In no concentration does an intra-arterial adrenaline infusion cause sustained vasodilatation in the forearm or calf. This is contrary to the general teaching that adrenaline dilates muscle blood vessels. Figure 74, 1B shows the effect of an intravenous infusion in which adrenaline is introduced into the general circulation as happens when it is secreted by the suprarenal gland In this case the transient vasodilatation is followed by a smaller sustained vasodilatation lasting till the end of the infusion. The forearm or calf blood flow during the sustained vasodilatation is about double the resting rate The cause of the sustained vasodilatation is not yet known. It is not nervous in origin for it occurs after the deep nerves in the forearm have been blocked (Fig. 74, 1C) and it occurs in acutely (but not in chronically) sympathectomised subjects (Fig 74, 1D). The rise in the mean blood pressure is too small to account for it It must be due to the local action of some vasodilator substances, either derived from adrenaline during its passage through the body or released from an internal organ or endocrine gland.

The action of adrenaline on the circulation in muscle may be summarised as follows During exercise and in certain physiological conditions its concentration in the general circulation will be increased [146] In these circumstances some other substances will appear in the general circulation which will dilate the muscle vessels The adrenaline itself will have no effect on the muscle circulation unless its concentration increases very suddenly. If so it may open the muscle vessels widely for the first one or two minutes

Figure 74, 2A shows the effect of an intra-arterial infusion of noradrenaline on the forearm circulation. The flow is reduced to about one third of its resting level for the duration of the infusion. The circulation in both skin and muscle are implicated The effect of an intravenous infusion is variable There may be an initial transient increase and for the remainder of the infusion the flow remains at the preinfusion level (Fig 74, B_1) or more often it is increased (Fig. 74, B_2) or occasionally decreased. The indirect vasodilator effect of intravenous noradrenaline is abolished and a vasoconstriction occurs if the deep nerves are blocked (Fig. 74, 2C) or if the arm is sympathectomised (Fig 74, 2D). It is therefore of nervous origin. The central effect producing this vasodilator action might be due to the rise in blood pressure acting via the baroceptors and the vasomotor centre.

In exercise and certain other physiological conditions the concentration of noradrenaline in the general circulation will be increased.[146] Owing to the

As far as we could tell it made no difference to the recovery of vascular tone whether the sympathetic was divided by preganglionic section or by ganglionectomy Two of our subjects had had preganglionic section on one side and ganglionectomy on the other. Figure 76 shows that contrary to the adrenaline sensitivity theory and to Cannon and Rosenbleuth's "Law and Denervation" (*see below*) there was no difference between the right and left

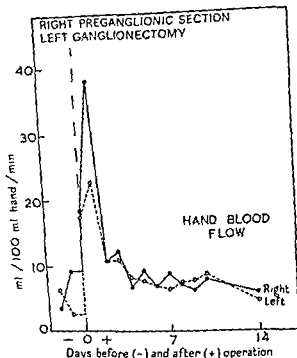


FIG 76

Changes in blood flow in the hands after sympathectomy *by preganglionic section on one side and by ganglion*ectomy on the other
The whereabouts of the sympathectomy made no difference to the circulatory changes
(*After Walker, Lynn and Barcroft* 155)

arms as regards the extent of the hyperaemia or the rate of its subsidence. This is quite in accordance with the fact that there is little or no difference between the long term clinical results of the two operations.[158, 159]

Various explanations have been suggested for the peculiar contrast between the behaviour of the blood flow and the digital temperatures:—

1. The blood flow in the *arterio-venous anastomoses in the digits* is permanently increased Elsewhere in the hands and feet it subsides so much that the overall flow through them is about the same as it was pre-operatively.

2. Owing to loss of venous tone each ml. of blood stays in the skin longer and so lose more heat.[160]

other hand the fingers remained warm. Rather similar results were recorded on feet. The increase in flow was less and two to three months after operation the foot flow was still doubled. The contrast between the subsiding foot blood flow and the sustained warmth of the toes is remarkable. As would be expected

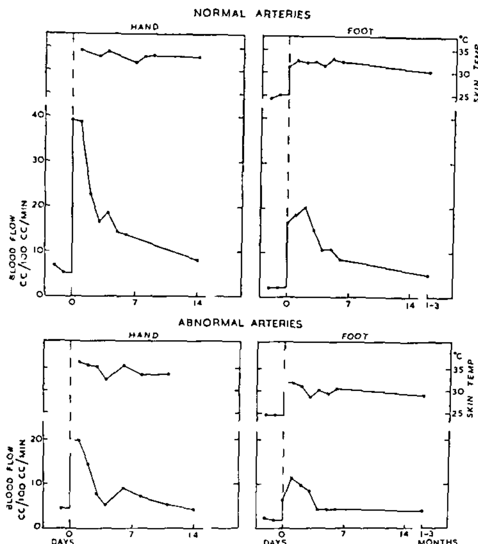


FIG. 75

Results showing the effect of sympathectomy on the temperature of the digits and on the blood flow through the hand and foot. The records were made in a comfortably warm environment.

(*Walker, Lynn and Barcroft* 155)

there was less vasodilatation in the hand and feet with diseased vessels Although the blood flow had returned to its pre-operative rate in a fortnight the fingers remained warmer than before operation. Two to three months after operation the blood flow in these feet was still doubled and, as Adson and Brown had reported, the toes were still very warm. (In one case the operation was followed by permanent hyperaemia in the feet. The clinical findings in this patient were reported by Lynn and Martin.[157])

changes for some weeks.[163] In one hyperhidrotic subject Aziz Ahmad found that warming the hand actually caused vasoconstriction and vice versa.[164]

At first sight the fact that the blood flow returns to about the pre-operative level in a short time seems to throw some doubt on the benefit likely to result

FIG. 78

Records of the effect of sympathectomy on the blood flow in the forearm and hand.

The [illegible] m; it w [illegible] may have [illegible] the

from sympathectomy However it must not be forgotten that the tests described above were carried out in a comfortably warm environment. In a cold environment sympathectomised fingers, no longer subject to strong central vasoconstrictor impulses, cool much more slowly than do normally ennervated ones.[32, 36] This is shown in Figure 77.

Figure 78 shows the effect of sympathectomy on the forearm circulation. Maximum vasodilatation takes place sooner than it does in the hand and foot, and is much smaller. Tone returns more quickly.[136] Recovery of tone after sympathetic denervation has also been reported in the vessels of the calf[165]

3. *Abolition of the cooling effect of sweating.*

It is a curious fact that the blood flow in the hands and feet does not increase to the maximum the instant after the sympathethic is cut and vasoconstrictor tone is released; the maximum is not reached till some hours later. Perhaps some vasoconstrictor substance enters the general circulation during the operation and prevents full vasodilatation from taking place at once. On

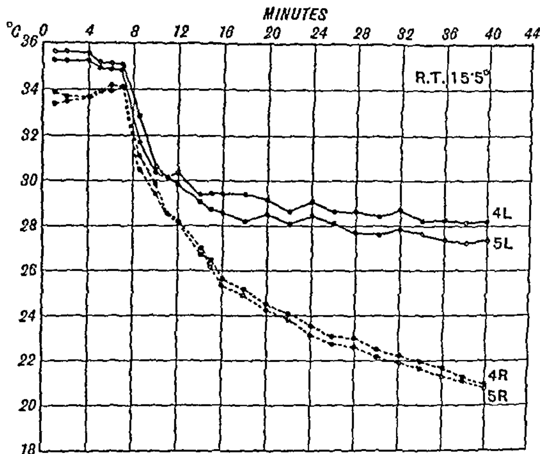


FIG. 77

Experiment in a cold room showing that sympathectomised fingers cool more slowly than normally innervated ones.
After half an hour's exposure to a room temperature of 15 5°C. the temperature of the fourth and fifth fingers of the left hand, which had been sympathectomised eighteen days earlier, was 6°C. above that of the corresponding fingers of the normally innervated hand (*Lewis and Landis* [36])

or about the fifth day after operation rather marked vasoconstriction was recorded in a number of the hands of our Raynaud patients, and one had a vasospastic attack (*see* Fig. 75—hands with diseased vessels). This only lasts a short time and has been reported by others.[161, 162] Govaerts thought it might be due to spontaneous discharge of impulses from the decentralised ganglion cells, since the temperature of the fifth finger rose 10°F. after ulnar nerve block. This vasoconstriction did not occur in any of our hyperhidrotic subjects.[133] The vessels in the hands are less sensitive to local temperature

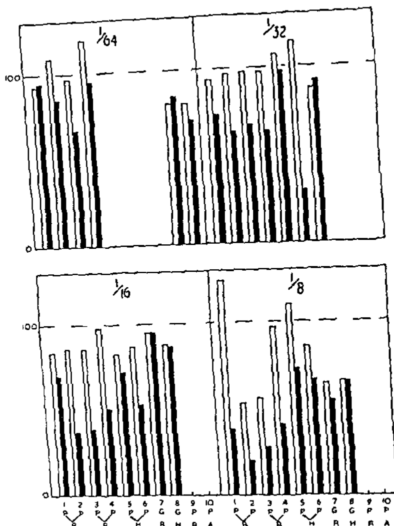


FIG 80

Results showing the effect of sympathe- . .
blood vessels
Abscissae. I
Ordinates:
percentage of
...
Shaded rectangles: pre-operative infusions
Black rectangles: post- ...
P, 's disease.

The ... the rate of
... adrenaline in micrograms per minute
Note increased sensitivity to adrenaline in hands 1 to 6 No increase in sensitivity in hands 7 to 10 (*After Duff*.[178])

and in those of the liver[167] and the ear drum;[168] indeed as Figure 79 shows the time relations for the recovery of the arterial blood pressure after total sympathectomy for hypertension are so like those for the recovery of tone in the vessels of the hand and foot as to suggest that intrinsic tone develops at much the same rate in the splanchnic blood vessels.[169]

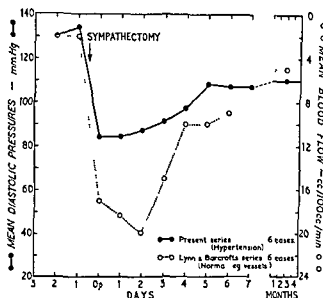


FIG. 79

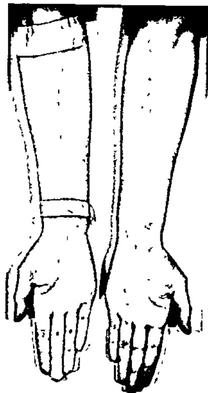
Results showing that recovery of sympathetic tone probably follows sympathetic denervation of the splanchnic blood vessels.

The means of the post-operative diastolic pressures, after thoracolumbar sympathectomy on the second side are compared with the means of the daily blood flows in the feet after lumbar sympathectomy (*Lynn and Barcroft's series* [154]) (*Longland and Gibb* [169])

The following hypotheses have been put forward to explain the development of intrinsic tone:—

1. Supersensitivity of the arteries to circulating adrenaline[170-173]
2. Decrease in the amine oxidase content of the arterial walls.[174]
3. Decrease in the acetyl choline content of the arterial walls.[175-177]

The adrenaline sensitivity theory is based on experiments showing that sympathectomised animal and human vessels are supersensitive to injected adrenaline and to adrenaline secreted during excitement or struggling. The skin temperature method was used so that quantitative results were not obtained Duff has recently re-examined the problem using the plethysmograph.[178-179] Blood flow in the hand was recorded before and during intrabrachial infusion of adrenaline ranging from $\frac{1}{64}$ to $\frac{1}{8}$ µg/min. Blood flow in the opposite hand not receiving adrenaline was recorded simultaneously and the results so obtained were used to correct the data for spontaneous bilateral fluctuations Figure 80 shows the results obtained in ten hands each



A



B



C

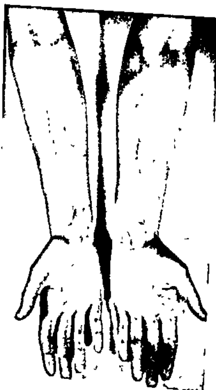


FIG 81

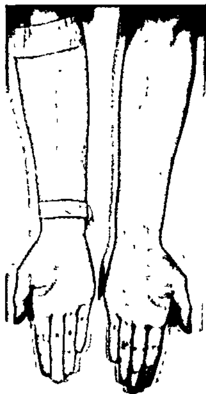
Infra-red photographs of the forearms [illegible]
(A), and forty-[illegible]

tested before (shaded rectangles) and after (black rectangles) operation. Control experiment showed that a 25 per cent. reduction in blood flow signified a definite vasoconstrictor response. On this basis the mean reduction in flow for all adrenaline infusions was 9 per cent before operation and 35 per cent. afterwards. So far as the averaged results in the ten hands are concerned they confirm Smithwick *et al.'s*[171] finding of increased sensitivity to adrenaline after sympathectomy. However, as regards the individual hands only six (Fig. 80, Nos. 1 - 6 inclusive) had become supersensitive Although the blood vessels in the other four hands were not supersensitive to adrenaline the post-operative hyperaemia in these hands had subsided and the blood flow had returned to nearly the pre-operative rate. It follows that the adrenaline supersensitivity hypothesis cannot explain the development of intrinsic tone after sympathetic denervation.

It is interesting to recall that Cannon did not believe that the recovery of tone was due to adrenaline supersensitivity. He gave two reasons for this. The first was based on observations on the cat with the heart rendered supersensitive to adrenaline by sympathectomy. In these cats the heart rate was not decreased by inactivation of both suprarenal glands, and he concluded that the amount of adrenaline in the blood under resting conditions must be insufficient to account for the regain of vascular tone Cannon's other experiment was on the effect of adrenaline on the smooth muscle of the stomach wall In the cat adrenaline inhibits this muscle. After sympathectomy the tone of the stomach wall did not decrease as would have been expected on the adrenaline supersensitivity theory, on the contrary it increased remarkably. He therefore thought it unsafe to attribute the regain of tone to adrenaline sensitisation [180]

We may now consider the amine oxidase hypothesis Burn and Robinson[174] found that the amine oxidase content of the cat's limb decreases after sympathectomy. If this happened in the walls of human arteries it might decrease the rate of adrenaline destruction and account for adrenaline supersensitivity and the return of intrinsic tone There are two objections to this hypothesis. First that the amine oxidase content of rabbit's arteries is unaltered by sympathectomy[175, 177] and therefore it is by no means certain that it would be reduced in man Second and more important as we have just seen the adrenaline sensitivity hypothesis cannot explain the development of intrinsic tone.

As a matter of fact the concentration of noradrenaline in the blood of the resting human subject is probably about four times as much as that of adrenaline[181] so that the notion that recovery of tone is due to supersensitivity to noradrenaline must be considered. Duff[182] has recently tested the sensitivity of the blood vessels of the hand to noradrenaline before and after sympathectomy. Although many do become supersensitive after operation some do not. It is therefore unsafe to consider the return of tone can be due to noradrenaline supersensitivity


A


B


C



The acetyl choline hypothesis is based on experiments on the vessels of the rabbit's ear.[175-177] These vessels normally contain acetyl choline which tends to cause vasodilatation. For some unknown reason the presence of this acetyl choline seems to depend on the integrity of the sympathetic nerve fibres. It disappears about three days after sympathectomy and its absence is believed to explain why the vessels become supersensitive to vasoconstrictor substances. Armin and Grant have found acetyl choline in human digital arteries a few hours post mortem. The idea that the return of intrinsic tone in human vessels may be due simply to decrease in the amount of acetyl choline in the vessel walls is certainly most attractive. The action of atropine raises a difficulty. According to the acetyl choline theory the widely dilated condition of the vessels in the hands of a normal subject during indirect heating must be due to the action of an abundance of acetyl choline in the vessel walls. It follows that the administration of atropine would be expected to reduce this vasodilatation. In fact large doses of atropine have no effect on the circulation in the vasodilated hand.[28] However the difficulty is not unsurmountable for several instances are known of responses to acetyl choline which are not blocked by atropine.[183]

Some other effects of sympathetic denervation must now be mentioned The first is its effect on the rate of tissue fluid formation in the forearm. This has been recorded before and twenty-four hours after operation in six subjects.[184] The results show that sympathectomy does not affect the rate of tissue fluid formation although as we have already seen the rate of the blood flow is greatly increased (Fig. 78). This paradox cannot be explained. Nor do procedures such as intravenous infusion of adrenaline, deep nerve block and indirect heating affect tissue fluid formation although they too increase the forearm blood flow. On the other hand muscular exercise and local heating increase both tissue fluid formation and blood flow.[187]

Figure 81 shows that sympathectomy releases vasoconstrictor tone in the veins.[188] It will be remembered that this was discovered many years ago by Lewis and Landis[30] (page 140).

The effects of sympathectomy described above have all been due to section of efferent fibres. In the cat and dog afferent fibres are divided too when the sympathetic connections of the limb are severed.[189-192] The implications of this in man may be of great importance Evidence of sensory fibres in the lumbar sympathetic chain has recently been obtained[193-195] This is shown in Figure 82. A few seconds after the application of radiant heat to the skin of normally innervated legs vasodilatation in the hands was recorded with plethysmographs. This vasodilatation was absent in these same legs after lumbo-dorsal sympathectomy. This was believed to be due to section of afferent fibres in the sympathetic chain, fibres concerned with the regulation of vasomotor tone and possibly with heat regulation. Further evidence of afferent fibres in the human sympathetic was obtained by the same authors

by direct stimulation of the sympathetic chain during lumbar sympathectomy.[196] Paradoxically this caused vasoconstriction in the hand. Now that it is known that the human sympathetic contains afferent fibres which are divided at sympathectomy further work is needed to classify their functions.

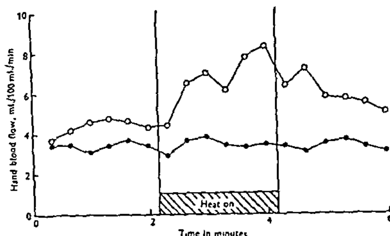


FIG. 82

Results showing that the sympathetic chain probably contains afferent fibres from the skin of the lower limbs.

Blood flow changes in the hand caused by the application of radiant heat to the normally innervated leg (circles) and to the contralateral sympathectomised leg (dots). Averaged results of nine experiments on three subjects (*Cooper and Kerslake.*[194])

Does preganglionic section sympathectomise the limbs completely?—This has been investigated by vasomotor and submotor tests on seventeen limbs. The tests were done within six months of operation.[197] In the vasomotor tests the blood flow in the hand was estimated before and after raising the body temperature to about 100°F. to release sympathetic vasoconstrictor tone. The result was called the heating ratio and was the ratio $\frac{\text{final blood flow per 100 ml. hand}}{\text{initial blood flow per 100 ml. hand}}$ In a normal subject releasing sympathetic tone increased the blood flow in the hand from about 4 to about 20 ml./100 ml. hand/min so that the heating ratio was about 5. This is shown in Figure 83 on the left hand side of the upper part of the diagram. In the completely sympathectomised limb releasing central vasoconstrictor tone could not have any effect on the blood vessels in the hand and the heating ratio would therefore be 1. Figure 83 shows that all of the seventeen hands had heating ratio of about 1 and therefore the Smithwick operation had in fact achieved a complete sympathectomy in every case. From the standpoint of the vessels of the hand neither the intervertebral ganglia[198] nor the intermediary ganglia[199] nor any other pathway[200, 201] could have been of any functional significance. The completeness of the sympathectomy in these limbs was then examined by the sudomotor test. In this test the resistance to the passage of a current through

the skin was measured (*a*) in the little finger in which sweating had previously been prevented by blocking the ulnar nerve (control skin), and (*b*) in the middle finger and thumb in which sweating had been excited as far as possible by raising the body temperature (test skin). The current strength in the control skin was subtracted from the current strength in the test skin and the result was called the current difference, *i.e.* (*b*) - (*a*). In normal subjects stimulation

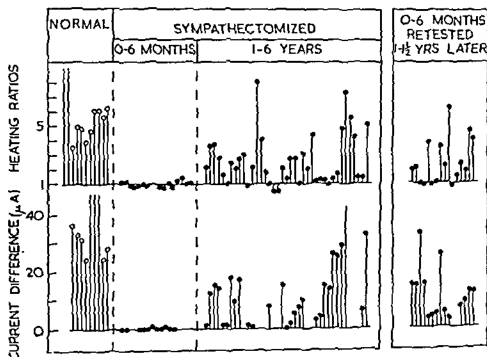


Fig. 83

Results of vasomotor and sudomotor tests performed on fifty-six limbs after sympathectomy, arranged from left to right in order of time interval between operation and testing.

Vasomotor and sudomotor reflexes were absent in limbs tested six months or less after operation, but present in limbs tested one to six years after operation The results show that the sympathetic nervous system re-establishes connection with the blood vessels in the hands and the sweat glands in the pads of the fingers and thumb. (*After Barcroft and Hamilton.*[191 and 201])

of the sweat gland in the test skin by warming the body increased the amount of moisture in it and lowered its resistance so that it passed 20 - 50 microamperes more than the control skin. This is seen in Figure 83 on the left hand side of the lower part of the diagram. In the completely sympathectomised subject impulses from the sudomotor centre in the brain could not reach the test skin, both test and control skin would be equally dry and consequently the current difference would be 0. Figure 83 shows that all the seventeen hands so tested had current differences of about 0 and therefore the operation must have achieved a virtually complete sympathectomy of the skin of pads of the middle fingers and thumbs of every one of these patients

When the operation is performed for vascular disease, as it usually is, the vasomotor test is the more relevant and its results indicate the completeness

of sympathectomy of the blood vessels of the hand. When the operation is performed for excessive sweating the sudomotor test is the more relevant: its results accord with the good clinical results obtained by Haxton.[202] The persistence of a few sympathetic fibres to the sweat glands has been demonstrated by more delicate methods than those used in the investigation just described. However the results of such delicate sudomotor tests are relatively useless for assessing the completeness of the denervation of the blood vessels of the hand.[32]

The completeness of the sympathetic denervation of the hand following the more extensive operation of cervico-dorsal ganglionectomy has not been investigated so thoroughly by us, but there can be no reason to suppose that the result would not be just as good. So far as we are aware, no results have been published in which the plethysmograph has not been used to investigate the results of lumbar sympathectomy. This should be done.

Does recovery of function occur eventually in sympathectomised hands?—Figure 83 also shows the results of vasomotor and sudomotor tests done on fifty-six hands between one and six years after operation (including the sixteen hands tested within six months of operation) all of which were retested again later.[203] As will be seen vasomotor and sudomotor reflexes were obtained in many of these hands and central connections must have been re-established, at any rate to some extent. Prior to operation many of these hands had had frequent and severe vasospastic attacks yet these had not recurred since. It seems unlikely that the vasomotor centre could have regained much of its former influence upon these vessels. The recovery of voluntary muscular movement after motor nerve injury is generally far from complete. Just how sympathetic connection is re-established is not known Perhaps by regeneration If so the fibres would have to bridge a gap of about an inch. An experiment of Lee's[204] shows that in the cat sympathetic fibres have remarkable regenerative powers. Lee cut the cat's cervical sympathetic and fixed the ends so that there was an inch of muscle separating them. Nine months later stimulation of the proximal portion caused dilatation of the pupil and retraction of the nictitating membrane. Another explanation of the reappearance of the sympathetic reflexes is that a new path begins to function above the level of T.2. This happens in the sympathectomised cat[205]

H. B.

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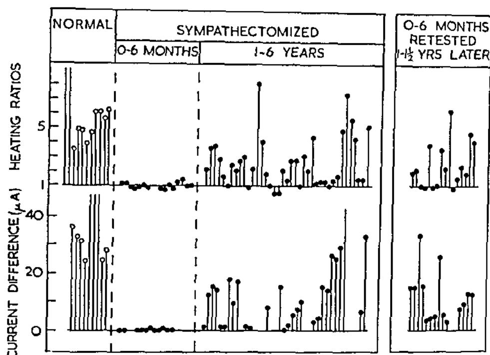


FIG. 83

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Vasomotor and sudomotor reflexes were absent in limbs tested six months or less a ... years after operation
The ... establishes connection
with ... ds in the pads of the
on.[197 and 203])

of the sweat gland in the test skin by warming the body increased the amount of moisture in it and lowered its resistance so that it passed 20 - 50 micro-*amperes more than the control skin. This is seen in* Figure 83 *on the left hand* side of the lower part of the diagram. In the completely sympathectomised *subject impulses from the sudomotor centre in the brain could not reach* the test skin, both test and control skin would be equally dry and consequently the current difference would be 0. Figure 83 *shows that* all the seventeen hands so tested had current differences of about 0 and therefore the operation must *have achieved a virtually complete sympathectomy* of the skin of pads of the middle fingers and thumbs of every one of these patients.

When the *operation is performed for* vascular *disease*, as it usually is, the vasomotor test is the more relevant and its results indicate the completeness

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tered for occasionally vascular changes have followed prolonged ergotamine therapy of migraine and jaundice urticaria. Intramuscular and intravenous injections have on occasion been followed by gangrene in a limb or in the buttock and deep venous thrombosis sometimes follows the injection treatment of varicose veins. Family or personal history of syphilis is sometimes available.

The age, the sex and the occupation of the patient may assist in the diagnosis of the disease which is present. In new-born infants congenital syphilis and "non-specific symmetrical digital gangrene" are the likeliest causes of vascular insufficiency; in the older child, hereditary cold fingers is the commonest vascular disease and Raynaud's phenomenon in the adolescent female; in the young male *thromboangiitis obliterans* is the usual cause of vascular disease whereas after the age of forty atherosclerosis, diabetes and acquired syphilis (rare now) are the commonest offenders. The dictum is worth remembering that a diagnosis of Buerger's disease in the female or Raynaud's disease in the male is usually wrong. Occupation should always be noted, especially with regard to the use of vibrating tools[17] and exposure to cold atmospheres; cold storage workers may present with manifestations of unexplained cold injury. Vocations necessitating prolonged periods of standing may be associated with varicose veins.

The importance of a careful review of the general systems of the body cannot be overemphasized Atherosclerosis is seldom a localised disease and exertional dyspnoea and angina are not uncommonly present in the patient complaining of intermittent claudication. In temporal arteritis and polyarteritis nodosa constitutional symptoms often predominate. The urine may reveal the signs of diabetes or nephritis in a patient with oedema. In unilateral lymphoedema and deep venous thrombosis an assessment of bowel and genital function should be made to rule out rectal and pelvic tumours. The association of Raynaud's phenomenon with systemic diseases should be remembered as well as the aggravation of peripheral vascular complaints by anaemia. Many of these associations will be revealed by an adequate review of major system functions.

Once the story of the patient's illness has been ascertained, a careful enquiry into past and family history has been completed and the general systems reviewed, physical examination is begun. A general physical examination is always carried out, with emphasis on the cardio-vascular system. The blood pressure is obtained in both arms and in some instances it should be obtained in the legs also. Especially when hypertension is present the retinae should be examined. Every vascular surgeon should be capable of examining the retinae as nowhere else in the body can the peripheral blood vessels be seen so directly and in many cases the status of the retinal vessels is a good index of vascular structure elsewhere in the body. Examination of the regional lymphatic system and palpation of the spleen and liver are essential

CHAPTER IV

CLINICAL EXAMINATION IN PERIPHERAL VASCULAR DISEASE

"An ischaemic limb resembles the inhabitants of a beleaguered northern town. With supplies diminished or cut off the inhabitants can keep up normal appearances for a little time, then they begin to starve, to feel cold, their faces become pale or blue, they are less active, and as conditions become worse they either become apathetic or complain loudly to those in authority. In the human limb there is absence of arterial pulsation, lowering of surface temperature, pallor or cyanosis, anaesthesia and pain" (Blackwood).[4]

IN disorders of the peripheral circulation, as in any disease complex, a careful enquiry into the symptoms of the patient will go a long way towards establishing the diagnosis and in some instances a precise knowledge of the symptoms alone will be the only method of making the diagnosis. It thus follows that the history is one of the most important parts of the entire examination The surgeon who allows the patient to describe the onset and the progress of his trouble will be certain not to miss information which often contains fundamental clues to the diagnosis For example a careful elucidation of the mode of onset, the site and the severity of pain in an extremity will often tell the examiner as much about the state of the circulation in the limb as will the physical examination, which may be merely confirmatory

The importance of a complete enquiry into the past illnesses of the patient must not be overlooked. The mention of past swelling, discoloration or pain in a leg must be thoroughly investigated for closer questioning may reveal a story compatible with deep venous thrombosis. Often a patient will remember the prolonged hospitalisation following illness, pregnancy or operation but will overlook a thrombotic episode which perhaps had not been explained to him. A past history of undue exposure to cold or damp (" cold injuries ") may throw light upon a hitherto unexplained vasospastic disorder. The mention of trauma, no matter how trivial, must always be kept in mind as it may clarify an unexplained thrombosis, the appearance of an aneurysm or a vasomotor disorder of the Sudeck type. Thus attention may be directed to the solution of the problem by searching the patient's past history for relevant clues.

The family history is important in such conditions as hereditary cold fingers and Milroy's oedema which are always inherited, and atherosclerosis and varicose veins and ulcers, which tend to run in families. The use of tobacco should be noted. A note should be made of drugs taken or adminis-

denoting fifty feet or less, the former a cramp which can be "walked off" as the metabolites of working muscle increase muscle blood flow; Grade II claudication is intermediate between the other two. Although such a grading has the merit of simplicity it is better to determine the absolute distance or work ability by means of the treadmill running at a standard rate or, if this is not available, by ergometry. A patient's figures for "claudication distance" are unreliable, for they depend on so many personal and environmental variables which cannot be assessed.

The usual situation of intermittent claudication is the calf of the leg and most commonly the medial head of the gastrocnemius. The small muscles of the foot or the muscles of the thigh and the buttock may be affected. This last muscle group is specifically involved in obliteration of the common iliac artery and its involvement may lead to a mistaken diagnosis of arthritis of the hip. Claudication in more peripheral muscles may present to the orthopaedic surgeon as foot or ankle strain. The muscles of the forearm or hand may claudicate so severely that the patient cannot write, but intermittent claudication in the upper extremity is uncommon, as is obliterative disease of the major arteries in the arms. In the younger age groups it is most commonly an indication of thromboangiitis obliterans. In atherosclerosis in the elderly, or after arterial embolism, weakness rather than pain is the usual residuum, but this depends upon the level of the obstruction and the degree of activity.

The only other site in which intermittent claudication is known to occur is the heart, where it is known as angina pectoris. It should be emphasized here that it is not at all uncommon to have angina pectoris and intermittent claudication in the same patient.[16, 20] This is not surprising, for in most instances the peripheral ischaemia is but the predominant manifestation of a generalised vascular disease. It may not be until the peripheral claudication has been improved that the symptoms of anginal pain become manifest. The relatively benign peripheral intermittent claudication is thus in a sense a protection against overwork of the ischaemic heart muscle.

Although most patients complain of pain with exercise in one limb only, careful study will reveal that both legs are affected by the obliterative arterial disease in most instances This is due to the cramp in the worse leg preventing the patient from walking sufficiently far to produce the limp in the better limb. In such instances testing of the individual limbs by ergometry will reveal the deficiency in the presumed healthy member. It is important to know this, so that the patient can be warned that relief of the pain in one limb may only lead to the other limb becoming exposed to unusual strain with the consequent development of symptoms in it.

Intermittent claudication is virtually always an accompaniment of obliterative disease of a major artery in the involved limb.[26] Rarely it may arise in severe anaemia[20] in the presence of patent vessels but more commonly anaemia in obliterative arterial disease aggravates a circulation already organically deficient. Intermittent claudication may follow severe

Before detailed discussion of the various signs and symptoms of peripheral vascular disorders there are a number of investigations that are always performed. A fasting blood sugar and urine analysis are always performed to exclude such conditions as diabetes and nephritis. A complete blood examination is required for the detection of anaemia and leukaemia, and Wassermann and Kahn tests are done. In most cases a chest X-ray is obtained and in special instances radiographs of the thoracic inlet are performed. An electrocardiogram is desirable in patients who suffer from obliterative arterial diseases and essential when angina, exertional dyspnoea or hypertension is present. Special examinations such as arteriography and tests of the capacity of the vessels to dilate are performed when it is felt that the information that they may supply will aid in the handling of the individual case. Should the general enquiry and examination have cast suspicion on some other system of the body a detailed investigation of that system is completed before the peripheral circulatory disorder is dealt with.

The commonest clinical features of peripheral vascular disease are pain, colour changes, temperature changes, absence of arterial pulsations, swelling, ulceration, and atrophy of tissues. These and other manifestations of ischaemia will be discussed now in some detail.

INTERMITTENT CLAUDICATION

This term stems from the Latin verb claudicare, meaning to limp, and intermittent limping is the commonest complaint in occlusive vascular disease. The variety, the site and the severity of this manifestation of ischaemia are good gauges of the degree of vascular supply in an extremity and give, as well, some clue to the diagnosis of the underlying disease in an occlusive rather than vasospastic arterial disorder.

Intermittent claudication was first described by the French veterinary surgeon Bouley[5] in 1831 as a cause of recurrent limping in horses. This was found to be associated with obliteration of the main artery of the leg. The syndrome was soon recognised in man.[6] With rare exceptions it indicates some obstacle to the free flow of blood to the muscles of the affected limb. The pain is diffuse, dull, continuous so long as exercise proceeds and usually described by the patient as a " cramp " or a " knot " in the leg. It increases in intensity until the discomfort is so great that the patient must desist from the exercise causing it. Since the exercise is usually that of walking the patient must stop to rest; when he stops the pain gradually goes away only to return when walking is resumed. The distance that can be walked before the pain occurs is known commonly as the " claudication distance " and is a fair gauge of the severity of the vascular obliteration in the limb. The amount of exercise necessary to produce the pain may remain remarkably constant or it may become progressively less as the disease process advances and the relative ischaemia of the muscles becomes more marked. Intermittent claudication has been graded by some authors[6, 22] from Grade I to Grade III, the latter

sitting up in bed clasping and rubbing the affected leg and begging that it be amputated as soon as possible. A less severe type of rest pain occurs in the absence of trophic lesions and has been termed "pretrophic pain."

A less common type of rest pain is that due to ischaemic involvement of the nerves in the limb. Examination of nerve trunks from amputated limbs may reveal Wallerian degeneration and excessive perineural fibrosis.[2, 21] These degenerative changes are proportional to the degree of ischaemia. Since there is no evidence of inflammation this condition is best termed ischaemic neuropathy rather than ischaemic neuritis. Usually a dull, constant ache is present in the limb and this is interrupted by severe spasms of sudden, excruciating pain which seldom follow any anatomical nerve distribution but tend to be diffuse. These exacerbations of pain may shoot from one end of the limb to the other, they are unrelated to exercise and are more frequent at night.

Rest pain must be distinguished from the pain of some other vascular disorders. Acute arteritis may be painful if the involved artery is superficial, as in temporal arteritis. The overlying skin is usually hyperalgesic in such instances and it is irritation of this rather than the artery itself which is the cause of the acute pain. Though the acute inflammatory stages of Buerger's disease are seldom appreciated by the patient, occasionally a deep-seated ache may be remembered. A similar situation exists with respect to deep venous thrombosis; although this is seldom acutely painful in itself, if the associated arterial spasm is severe, as in phlegmasia caerulea dolens, pain may be acute. In superficial recurring thrombophlebitis or "thrombophlebitis migrans" too the pain is usually mild, but if the involved vein lies across the ankle or wrist joint movement exaggerates the distress and pain may be severe.

Sudden arterial occlusion, as in embolism and thrombosis, has been said classically to be accompanied by the abrupt onset of acute pain in the limb In point of fact only about half of such cases are accompanied by more than a feeling of pins and needles in the extremity and in an equal number the onset of the symptoms, whether paraesthesia or pain, is gradual The theories behind the mechanism of pain in acute arterial occlusion are discussed in Chapter XII.

INTERMITTENT PAIN UNRELATED TO EXERCISE

Intermittent pains of varying types occur in response to exposure of the limb to cold, to warmth or to dependency. Discomfort, rather than actual pain, occurs in patients subject to Raynaud's phenomenon when they expose their susceptible hands to cold. In the phase of spasm, numbness or "woodenness" is complained of and in the phase of rubor the feeling of intense pins and needles and formication may be very distressing A similar situation exists in the recovery phase in acrocyanosis. Since Raynaud's phenomenon is nearly always secondary to some general systemic or vascular disease, complaint of severe pain is more likely to be due to the underlying condition.

arterial spasm precipitated by cold or by exercise,[11] and in these circumstances the peripheral pulses may be impalpable. When, however, the patient is re-examined at rest in a warm environment all the major pulses return and no underlying obliteration is detected by careful vascular and neurological examination. Ordinarily the site of the claudication and the amount of exercise necessary to produce it are good indices of the level and extent of the arterial block. The exact state of the vessels can be determined by arteriography where it will be noted usually that the arteries supplying the muscles are fewer in number, that they "tail off" before being distributed to the muscles, or that their origins are blocked in the occluded segment so that collateral vessels have to carry the muscular circulation. Although these vessels may be capable of carrying a sufficient blood supply to the muscles at rest they cannot increase the circulation sufficiently to meet the demands of even moderate exercise, and pain develops.

Intermittent claudication has been shown to result from the collection of acid products of muscle metabolism.[13, 14] Normally these are removed during exercise by a greatly augmented circulation. There is some evidence to suggest that these metabolites are produced in excess in the ischaemic limb, but it appears more likely that they are produced in normal quantities but that the deficient circulation cannot remove them and they accumulate to a level sufficient to stimulate somatic nerve endings in the muscles with the production of the pain and cramp of intermittent claudication. Similar pain can be produced in a normal limb when muscular exercise is performed in the presence of proximal arterial occlusion.[9] The chemical constitution of the actual acid metabolite responsible for this phenomenon is not known but has been called "Factor P." The fact that local nerve block will relieve or prevent the pain of intermittent claudication and that sympathectomy or sympathetic block is rarely beneficial shows that the somatic element is predominant. Any relief of pain after sympathectomy is due to the increased circulation to the muscles rather than to the interruption of pain fibres in the sympathetic pathways from the limb.

REST PAIN

The development of pain in an ischaemic limb while at rest is an ill omen. It is evidence of advanced ischaemia and is most severe when the ischaemia is associated with sepsis, ulceration and overt gangrene. This constant, deep pain is most often encountered in thromboangiitis obliterans but it is not unusual in atherosclerosis, particularly when the atherosclerosis is associated with diabetes; not only are the effects of atherosclerosis in diabetes quite commonly complicated by the presence of neuritis, but diabetes predisposes to infection

The victim of rest pain will offer the information that he has had to sleep in a chair, or with the leg hanging over the side of the bed outside the bedclothes in order to get any rest at all. When seen the patient is in poor physical shape—a gaunt, unshaven, chain-smoking, hollow-eyed spectre

COLOUR CHANGES

Lewis's classic monograph[12] should be consulted for greater details of the knowledge of the peripheral circulation to be gained from clinical observation of the colour of the skin. Suffice it to say here that skin colour is a good index of the peripheral blood flow when the normal responses to environmental conditions are known Without a knowledge of the normal responses intelligent clinical interpretation is impossible.

Generally speaking the colour of the skin is a good index of the rate of blood flow in it and usually also of the flow in the deeper tissues. If the arterial blood is fully saturated upon arrival in the capillary bed it loses oxygen progressively in its passage to the venous side of the circulation. In the normal limb the amount of oxygen given up is seldom sufficiently excessive to produce discoloration of the skin. In the final analysis the amount of oxygen removed from the blood in the affected limb determines the skin hue and so the importance of temperature in colour changes of the limb can be appreciated Cold favours the retention of oxygen by the blood whereas warmth favours the rapid dissociation of oxygen so that cyanosis develops more rapidly in a warm limb than in one cold at the time of arterial occlusion.

It is natural for the skin of a normal limb to show cyanosis over quite a wide range of environmental temperatures since external cold causes arteriolar constriction and a slowing of blood flow in the skin. Thus it becomes of some importance to be able to differentiate between physiological and pathological grades of dermal discoloration. The presence of cyanosis indicates a decreased rate of blood flow but careful examination may be necessary to determine whether it has an organic basis, or whether it is merely a physiological response to environmental conditions. Other causes of cyanosis, heart disease and methaemoglobinaemia, for example, should of course be kept in mind

Similarly, the return of colour to a part after pressure must be carefully interpreted. When skin is compressed it blanches and when the pressure is released the normal colour rapidly returns, but a rapid return of colour to an area previously blanched is more dependent upon the capillary (or capillary and venous) blood pressure in neighbouring area than on arteriolar filling. Thus rapid obliteration of a blanched area can occur in the face of severe arterial occlusion; thus return of colour may be [illegible] ependent ruboric [illegible]

[illegible] limb is affected [illegible] relation of the part to the horizontal. It is obvious that the examiner must first be cognisant of the possible colour changes that occur when a limb with a normal circulation is elevated or allowed to hang down When examining the upper limbs it is a good thing to compare the changes in the examiner's hands with those in the patient's Normally there is little change of colour when the normal hand is held above the head and such pallor as there is is lost rapidly and uniformly with return

Attacks of a burning type of pain, usually precipitated by exposure to warmth, following dependency of the limb or less commonly exercise, are characteristic of erythralgia. This pain is exaggerated by stretching the skin and is usually relieved by exposure to cold. The attacks resemble those of tic doloreux in that a variety of stimuli will precipitate an attack in susceptible tissues. There is usually a local fault to be found as the causative agent in producing tissue susceptibility and the process is often inflammatory or post-inflammatory in nature, as it is in frostbite and Sudeck's atrophy. Similar attacks of burning, lancinating pain occur in limbs the seat of glomus tumours or as a part of the picture in causalgia.

The bursting pain and heavy discomfort in a limb the seat of chronic venous insufficiency is quite characteristic as it is produced only by dependency and is relieved by rest and elevation. The limb is usually oedematous and often shows a chronic venous ulcer. The pain is occasionally exaggerated in bed at night, a finding which is probably due to the vascular relaxation which is brought on by sleep and which leads to congestion in the limb. If there is coexistent arterial insufficiency and ulceration, similar night pain is common. In lymphoedema, without venous insufficency, pain is a rare complaint but heaviness and aching are common.

Nocturnal cramp[25] is a sudden, acute muscle cramp which begins whilst the patient is in bed or at rest and is usually the result of an exaggerated involuntary tonic contraction of a muscle or group of muscles. This contraction squashes blood vessels and arrests the circulation so that although the pain at first may be due to muscle spasm alone it is possible that ischaemia potentiates it later on. However, as soon as the spasm is relaxed the pain goes, so that ischaemia probably plays a minor rôle since one might expect a delayed relief of pain if ischaemia was important. The cramp is relieved by exercise which substitutes alternating contraction and relaxation for the continuing spasm. Nocturnal cramp is most frequent in the abductor group of the intrinsic muscles of the great toe and in the muscles of the calf. It is prone to develop in diseased muscle groups, in myopathies for example, but in normal muscles fatigue and cold seem to be important causative factors It should never be confused with the cramp of intermittent claudication for it arises during rest and is relieved by exercise whereas the pain of intermittent claudication arises during exercise and is relieved by rest. Although nocturnal cramp is not due to vascular insufficiency it is a not uncommon complaint in individuals who suffer from vascular insufficiency. The exhibition of either quinine (5 grains), dilute hydrochloric acid or Priscoline (25 - 50 mgms.) before retiring, are effective in alleviating this troublesome condition. The effectiveness of Priscoline, a myoneural paralysant, may be due to a damping effect at the myoneural end-plate.

as a rubro-cyanosis (Figs. 84B and 85). Although it is usually confined to *the forefoot* it may involve the whole foot and the ankle and indicates a *markedly* impaired rate of blood flow. It may be graded from I to IV according to its severity and thus roughly indicates the degree of circulatory stagnation

In chronic venous insufficiency circulatory stasis results from varying degrees of obstruction to the venous outflow from the limb The slowed rate of circulation causes excessive amounts of oxygen to be extracted from the venous blood and cyanosis is a common feature of the condition. The cyanosis varies with the environmental state and is confined to the involved limb. Persistent symmetrical distal cyanosis, chiefly of the fingers and forefeet, is a characteristic of acrocyanosis and sometimes is confused with Raynaud's phenomenon.



FIG 85

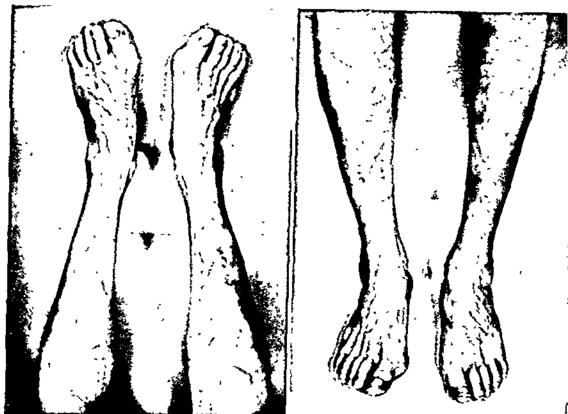
Dependent rubor in an elderly atherosclerotic

The classical sequence of colour changes in the digits in Raynaud's phenomenon are first pallor, then cyanosis and finally rubor, but these phases do not necessarily follow with orderly precision and often all three phases may be demonstrable in the same limb at the same time. In clinical practice the colour changes are seldom observed spontaneously and usually have to be artificially induced. This and the fact that the stage of pallor may be absent if the hands are dependent at the time of the attack probably account for most of the lack of uniformity. The clinical phases in Raynaud's phenomenon accurately indicate the state of the circulation in the part. The pallor in the phase of syncope is due to a virtual cessation of skin blood flow; the cyanosis in the phase of asphyxia in Raynaud's phenomenon, or in the persistent cyanosis of acrocyanosis, is due to circulatory stasis; the rubor of the recovery phases in both indicates an excessive rate of blood flow through the part

SKIN TEMPERATURE

The skin temperature of a resting limb depends upon the balance between the amount of heat brought to it by the blood and the amount of heat lost to its surroundings. If blood flow is reduced less heat is brought and the part becomes abnormally cool Many environmental factors may also influence the skin temperature so that isolated readings are valueless, but *when both limbs* have been carefully examined under similar conditions and *one is found* to be consistently colder than the other, it may be assumed that the colder member has a smaller cutaneous blood supply. Whether this

of the hand to the horizontal position. In the presence of arterial occlusic there is rapid emptying of the vascular bed and the distal arterial pressui is too low to keep the vessels filled against gravity so that pallor of varyir degrees develops (Fig. 84A). The limb may become cadaveric in appea ance and when returned to the horizontal the return of colour is patchy (delayed in proportion to the degree of vascular obliteration. In the low(limbs the patient lies supine with his legs supported at 90° to the horizonta



A FIG. 84 B

(*a*) Pallor on elevation and (*b*) rubor on dependency in a thirty-two year old man with bilateral thromboangiitis obliterans, and proven popliteal blocks

The presence of arterial occlusion is associated with a low intra-arterial pressure distal to the block and so gravity cannot be overcome and the feet assume a deathly pallor. This is most striking if the patient's contralateral limb is normal and can be used as a control. The degree of pallor is roughly proportional to the severity of the circulatory impairment and inversely proportional to the efficiency of the collateral channels.

With the information from elevation at hand the legs are then swung over the side of the bed and allowed to dangle loosely there whilst the rate of venous filling and the colour changes are noted. As in the hand, colour normally returns within a few seconds. In arterial insufficiency the return of colour is patchy and delayed often for a minute or more to be followed by an increasing depth of colour. The final colour in this condition is best defined

of hairs on the dorsum of the toes is a good index of the severity and the duration of ischaemia.[19] Hairs still present in the face of major artery occlusion indicate either that the course has been short or that the collateral circulation is good. The shape and form of the nails and the rate of growth depend upon the amount of blood being supplied and offer another index of



FIG. 86
Pulp and skin atrophy of fingertips in a man with Raynaud's phenomenon due to thromboangiitis obliterans



FIG. 87

adequacy of the circulation. The patient may offer the information that he needs to trim his nails less often than formerly.

The skin becomes glossy and parchment-like with loss of the print pattern and wasting of the subcutaneous tissues of the digital pulp (Fig. 86). This digital pulp atrophy leads to the finger or toe becoming pointed (Fig. 87) and atrophy of subcutaneous tissue elsewhere leads to the development of callouses over weight-bearing areas on the foot. These are not uncommon under the metatarsal heads and on the under-surface of the ... "Raynaud's Disease" and lon...
transformation may bec

is due to organic arterial disease or to abnormally increased arterial spasm cannot be determined without tests which depend upon the release of vasomotor tone. Normally there is a gradual temperature gradient from the proximal to the distal parts of a limb, the digits being the coolest part of the extremity. In occlusive vascular disease the gradual decline of cutaneous temperature towards the periphery becomes abrupt at the level at which ischaemia becomes pronounced. Sensitive instruments are not necessary to detect temperature differences since the dorsal aspects of the practised examiner's fingers can distinguish temperature differences as small as 1°C. It is essential that the examining fingers be warm. The patient may be able to give valuable information as to the degree and distribution of the coldness in the affected limb. Alterations in temperature and colour of a limb thus allow a fairly accurate estimation of its vascular supply to be made.

VENOUS FILLING

A segment of vein can be emptied by applying digital pressure at its distal end and stripping the blood from the segment disto-proximally. When the distal finger pressure is released, the collapsed vein refills rapidly if the peripheral circulation is normal. The rate of refilling is a rough index of the rate of blood flow in the limb and is of greatest value when it can be compared with an opposite normal limb under similar environmental conditions. A more accurate index is obtained by noting the speed with which veins refill when the feet are moved from elevation to dependency. Normally the dorsal veins of the foot fill within five to seven seconds of assuming the dependent position. Prolonged delay in venous filling is good evidence of the rate of arterial blood flow in the part—the more delayed the filling time the more complete the obstruction. The test must be interpreted with care when varicose veins are present since venous reflux may obscure the true rate of venous filling

In the ischaemic limb the superficial veins are usually collapsed, particularly if arterial occlusion has been sudden The presence of markedly dilated superficial veins should draw attention to the possibility of deep venous obstruction, thrombophlebitis for example, or compression of the veins by malignant glands or fibrosis. In such instances, and in the presence of arterio-venous fistulae, in which the intravenous pressure is very high, the venous distension persists even though the limb is elevated above the horizontal.

NUTRITIONAL CHANGES

Atrophy.—In chronic arterial insufficiency muscles, subcutaneous tissues, skin and skin appendages show the effects of long-standing or oft-repeated impairment of blood supply. These effects are most noticeable in the distal parts of the limb and specialised structures are especially susceptible to deprivation of blood supply. Thus diminution in the number or complete loss

afflictions tend to become chronic and recurrent because the arterial deficiency handicaps healing Similar infections may develop after the paring of corns or in blisters from ill-fitting shoes. In any recurrent infection of a finger or toe arterial insufficiency, diabetes and fungus infections must always be excluded These infections are seldom associated with constitutional symptoms.



Fig 89
Acute digital artery thrombosis, proven arteriographically, complicating "Raynaud's Disease"

Epidermophytosis probably occurs no more frequently in the ischaemic foot than in the normal but it is more likely to be sought and therefore discovered in the former.

Recurring superficial thrombophlebitis is a frequent accompaniment of thromboangiitis obliterans and like the latter its cause is not known. The skin overlying the involved vein becomes red and oedematous but suppuration does not occur.

Ulceration.—Superficial tissue loss in the legs is much more frequently due to chronic venous insufficiency than to chronic arterial insufficiency. In the arms ulceration due to chronic venous insufficiency does not occur and spontaneous tissue loss is always due to arterial disease. Long-standing "Raynaud's Disease" is often accompanied by patchy tissue loss of the finger tips (Fig. 88). In some instances it may deserve to be called gangrene

complete obliteration of the digital blood vessels can be shown by arteriography. Such scleroderma is strictly acral in distribution in contrast to the more generalised and facial distribution of primary scleroderma.

Muscle wasting can usually be detected and is most noticeable when comparative measurements are made of limbs only one of which is affected by arterial insufficiency. Atrophy of several centimetres of girth of the calf muscle is not infrequent but it is probable that part of the muscle atrophy in peripheral vascular disease is the result of disuse rather than ischaemia. In the foot,



FIG 88

loss of bulk of the intrinsic muscles of the sole and atrophy of the extensor digitorum brevis on the dorsum of the foot can often be appreciated A fine fibrillation in the involved muscles is additional evidence of ischaemia but this point can only be assessed in a warm environment since similar tremors can occur in response to cold even if the muscle circulation is normal. Similar muscle tremors and wasting may occur after nerve injuries and anterior poliomyelitis.

Chronic Sepsis.—Impaired blood supply to a limb undermines the resistance of the tissues so that paronychia and whitlow, arising spontaneously or following careless trimming of the toe nails, are common occurrences. These

A special type of ulcer has been described in patients with hypertension and is said to be the result of arteriolar degeneration. It arises on the anterolateral aspect of the lower third of the leg and tends to be small, bilaterally symmetrical, painful and frequently multiple. The diagnosis can only be made on the presence of hypertension and the absence of chronic venous and arterial insufficiency.

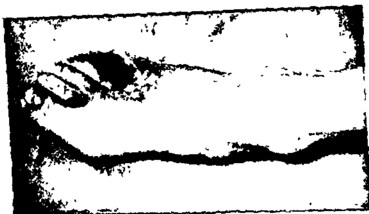


FIG. 91
Dependent rubor and gangrene in a twenty-seven year old man with thromboangiitis obliterans

The multiple, superficial ulcers of chronic chilblains (erythema induratum, Bazin's disease and perniosis) are discussed in detail in Chapter XVI. They commonly occur on the lower legs of adolescent and middle-aged females. The ulceration of chronic chilblains is multiple and is accompanied by swelling of the legs and enlargement of the regional lymph nodes. Bacteriological and pathological examination of tissue excised from an ulcer is usually necessary to distinguish ulceration due to specific infections, *e.g.* tuberculosis, from that of chronic chilblains.

Gangrene.—Massive death of tissue is the end phase of severe ischaemia and it varies with the site and extent of the arterial occlusion. Thus in "Raynaud's Disease" or frostbite only "thimbles" of tissue from the finger tips may be lost whereas in aortic embolism both legs may become gangrenous. There is no virtue in retaining the terms "wet" and "dry" gangrene as one may follow the other in the same limb and neither one constantly follows a specific type of arterial occlusion. Gangrene often follows ulceration. Atherosclerotic gangrene is *not* often accompan[illegible]
reaction [illegible]
predomir[illegible]
angiitis c[illegible]
[illegible] may be extensive and rest pain severe, particularly when a trophic lesion has preceded the onset of the gangrene.

(Fig. 89). As causes of chronic sepsis and ulceration of the fingers "Raynaud's Disease" (thrombotic digital artery occlusion[15]), Buerger's disease and cervical rib are responsible in that order of frequency. Large symmetrical ulcers, particularly if painless, should immediately turn one's attention to syringomyelia or some other spinal cord disorder.

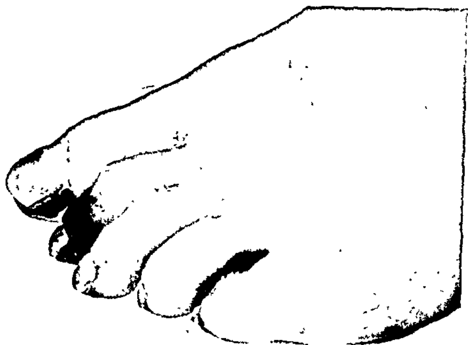


FIG. 90
Spontaneous gangrene in the foot of a forty-eight year old diabetic

In the leg the venous ulcer of chronic deep venous insufficiency, characteristically situated just above the medial malleolus, is by far the commonest ulcer encountered. Similar ulceration may follow primary varicose veins even in the absence of deep venous occlusion or disease. A history of a previous attack of thrombophlebitis is obtained from these patients often and a familial history of varicose veins nearly always. The presence of ulceration of the ankle in a young person with prominent varicosities and a warm limb may be due to an arterio-venous fistula.

Arterial ulcers may occur spontaneously after acute arterial occlusion, but usually they develop after trauma to the leg or foot. The accident may have been so trivial as to have been almost forgotten The traumatic ulcer arises at the site of the injury whereas spontaneous ulcers complicating acute arterial occlusion are most likely to be found on the anterolateral aspect of the limb These ulcers tend to be deep, indolent and, especially in thromboangiitis obliterans, accompanied by severe rest pain When a venous ulcer does not respond to treatment the presence of concomitant arterial insufficiency should be considered since the association of the two is not uncommon.

SWELLING AND OEDEMA

The oedema of chronic renal and cardiac diseases must be recognised and separated from that complicating deep venous insufficiency, lymphatic insufficiency and lipoedema. Nowhere is the patient's history more important than in the diagnosis of oedema since examination of the nature of the swelling is of limited value. The intermittency of angioneurotic oedema is characteristic. Localised swelling should suggest the presence of a local bone or soft tissue tumour whereas the rapid onset of unilateral swelling in a limb arouses the question of malignant obstruction of the regional lymphatics of that extremity. History of a unilateral swollen leg from birth may be the presenting complaint in arterio-venous fistula of congenital origin and cavernous lymphangioma of an extremity.

The oedema of deep venous insufficiency, acute or chronic, is at first pitting in nature and completely regresses with recumbency or elevation. The mode of onset and later the association of superficial varices, stasis dermatitis and gravitational ulcer differentiate the condition from chronic oedema due to other causes In their early stages all forms of chronic oedema are relieved by rest and elevation, and in all ultimate hypertrophy and fibrosis of the subcutaneous tissues occurs so that the oedema gives way to permanent hypertrophy and swelling of the limb. This swelling is often complicated by attacks of cellulitis—features seldom encountered in the post-thrombophlebitic limb where stasis ulceration and varices tend to predominate.

Oedema is seldom encountered in chronic arterial insufficiency except when rest pain has become so severe that the patient sleeps in a chair or with the leg hanging over the side of the bed. Gravitational oedema is liable to develop especially in young men with Buerger's disease or diabetic atherosclerotics Here the presence of such complications of ischaemia as sepsis and ulceration make the diagnosis relatively easy.

Lipoedema is a non-pitting, symmetrical swelling of the legs of women due to an increase in the amount of subcutaneous tissue rather than to an accumulation of interstitial tissue fluid. In most instances a history of thick ankles from early life is obtained but a recent gain in weight may be associated with the development of "swollen ankles" and the request for advice. Oedema is seldom marked but it is limbs such as these that appear to be unusually prone to develop areas of fat necrosis, characteristic of chronic chilblains. The patchy discoloration and the subcutaneous nodules of this condition may be felt.

ASYMMETRY OF LIMBS

Hypertrophy of the whole of a limb implies the presence of a congenital arterio-venous fistula whereas wasting and shortening of a limb suggest the residua of anterior poliomyelitis In the latter there is muscle wasting, atrophy and shortening of bone from lack of growth, and often contractures. Such a

Gangrene usually begins in the digits, and in arterial obstruction of the lower limbs most frequently on the under-surface of the fifth toe or the great toe unless it has been precipitated by trauma when it arises at the site of the trauma (Fig 90). When gangrene begins elsewhere than in a toe it is frequently preceded by blebs or blisters, especially if it occurs on the dorsum of the foot (Fig. 91). The usual course of untreated gangrene is a progressive proximal



Fig 92
Acute popliteal thrombosis showing massive gangrene and pitting oedema

extension In acute arterial embolism or thrombosis massive gangrene of a major portion of the limb may be apparent from the beginning (Fig. 92). Sudden gangrene in the fingers should make cervical rib suspect and although rare now tertiary syphilis should be excluded in symmetrical digital gangrene.

Gangrene occurs as a complication of a massive type of sudden deep venous thrombophlebitis known as phlegmasia caerulea dolens. This condition simulates femoral arterial embolism and has been explored under this diagnosis. Whether the gangrene is due to the massiveness of the venous thrombosis or chiefly to the severe associated arterial spasm has not been settled.

The ulnar artery is palpable just medial to the tendon of the flexor carpi ulnaris and it too can be traced a little distance proximally. The digital arteries of the fingers can be palpated in most instances at the bases of the fingers but it may be necessary to warm the subject and/or his hands first.

When doubt exists regarding the patency of the two main arterial branches at the wrist and at the ankle a simple test (Allen's) can be performed. The radial artery is occluded after the hand has been held aloft and exercised. When the hand is lowered it will become pink quite rapidly if the ulnar artery is patent but if the hand remains pale the ulnar artery is partly or completely occluded



FIG. 93
Positive Allen's test in a man with thromboangiitis obliterans

and the main blood supply to the hand is via the radial artery (Fig. 93). This can now be confirmed by releasing the pressure on the radial artery whereupon the hand will flush rapidly. A similar manoeuvre can be applied to the foot with respect to the dorsalis pedis and posterior tibial arteries. Doubt has been cast upon the value of this test since it may be positive in the absence of arterial disease.[3]

The carotid artery is easily felt in the neck and the temporal artery can be felt for just in front of the tragus of the ear. The value of examining the retinal arteries has already been mentioned.

The abdominal aorta may be quite impalpable in an obese individual whereas in a thin subject it may be palpable in its entire length The common iliac and external iliac vessels are subject to the same conditions but they should be carefully felt for when the femoral pulses are absent Visible and palpable pulsation of the intercostal arteries may be apparent in cases of coarctation of the aorta; these can best be observed by standing behind the patient who is bent forward at the waist in which position the pulsating intercostal arteries can be seen on the back.

position is considered to be due to an organically occluded artery, sometimes the absence of a standard pulse is normal for that individual.

The degree of impairment of pulsation is graded by the authors as Grade 0 to Grade III. Grade 0 indicates an absent pulse; Grade I indicates a pulse which can only be felt when the limb and body are heated; Grade II indicates a clinically diminished pulsation; and Grade III indicates a pulse of normal volume. The following vessels are felt for in every patient presenting with complaints referable to the peripheral blood vessels.

The femoral artery is easily felt in the groin just below Poupart's ligament as it lies over the head of the femur. In a thin individual it may be traced into Scarpa's triangle and rarely it may be palpated in Hunter's canal

The popliteal artery is normally difficult to feel, especially should the patient be fat. This deep-seated vessel can only be adequately felt if the muscles surrounding the popliteal fossa are completely relaxed. It is best felt with the patient prone and the relaxed leg passively supported at right angles to the bed while the popliteal fossa is palpated. In most instances the patient may be supine with the knee flexed and passively supported at a right angle while the fingers feel for the vessel behind. A similar manoeuvre can be carried out with the leg loosely dangling over the side of the examining table.

The dorsalis pedis is felt for in a line passing from between the bases of the first and second metatarsal bones to the mid-point of the anterior aspect of the ankle joint. It should be remembered that this vessel is normally absent in about 10 per cent. of individuals,[18, 24] so that its absence is not positive proof of arterial disease. If it is absent its function is usually served by the perforating branch of the peroneal artery as it comes through between the tibia and fibula above the extensor digitorum brevis

The posterior tibial artery is usually situated midway between the medial border of the calcaneus and the medial malleolus. In about 5 per cent. of individuals the posterior tibial artery is anatomically absent, being replaced by the peroneal artery.[18, 24] As with the dorsalis pedis, such anatomical variations are usually bilateral and this helps to distinguish whether a pulse is pathologically or anatomically absent.

The subclavian artery is felt for above the clavicle, or it may sometimes be felt in front below the middle of the clavicle The axillary artery can usually be palpated in the arm-pit. The brachial artery can be followed in most of its course unless the patient is obese or very muscular. Its course too is subject to anatomical variations. From its point of division at the elbow to the wrist pulsations of the vessels in the forearm are difficult to feel especially in heavily muscled subjects.

The radial artery is felt as it lies on the anterior surface of the radius just above the crease of the wrist. It can usually be traced to the back of the hand at the base of the first metacarpal bone as well as proximally in the lower third of the forearm.

CHAPTER V

METHODS OF INVESTIGATION OF THE PERIPHERAL CIRCULATION

IT may be stated at the outset that there is no test which will replace the information to be gained from a careful history and clinical examination of the patient and of the affected limb. Although most of the special tests aid in the confirmation of the diagnosis they are performed, broadly speaking, for two purposes only; first, to assess the potential state of the circulation in the affected limb, and secondly, to determine therefrom the therapeutic procedure most likely to afford the greatest relief and the best prognosis. There is as yet no single reliable test which will give this information. As his experience of vascular disorders increases the clinician becomes less dependent upon laboratory tests and fewer predictions will be made from them. Data obtained from any test must be carefully considered against the clinical picture before any conclusion relative to the individual case can be drawn.

The tests which have been employed in this laboratory will be discussed under several headings, more or less as we find them to be useful, simple and informative. A number of procedures which will be mentioned are no longer used because the information they give is of limited value or can be obtained by simpler methods. It is doubtful whether laboratory tests will ever be devised to replace clinical examination although strenuous efforts to discover tests that will do so are being made. The dictum " know your patient " must remain foremost and then ancillary tests can be viewed in their proper perspective.

Since peripheral blood flows and the methods used for their determination depend upon many factors it becomes necessary to minimise the effects of as many of the variables as possible. Not the least of these is environment. Ideally the study should be conducted in a room in which the temperature, humidity and air movement can be controlled. Such constant environment rooms are available but their expense limits them to special centres. For practical purposes a draught-free room which is quiet and which can be kept at a temperature of approximately 70°F. will suffice. The individual should be studied at rest, in the fasting state and in a constant position—preferably supine with the parts being studied kept at heart [illegible]

[illegible]

[illegible] in skin temperatures and blood [illegible] and alterations in other tests employed become significant when compared

Collateral or accessory arteries should be sought by palpating at the knee, ankle, elbow and wrist in the light of the normal anatomical variations even though collateral net-works in these regions, anatomically profuse, seldom become sufficiently large or pulsatile to be felt. At the wrist the vessel most frequently felt is the perforating branch of the anterior interosseous artery on the dorsum of the wrist. At the elbow the anterior descending branch of the profunda artery and the posterior ulnar recurrent artery are sometimes palpable. At the knee the superior medial and lateral genicular arteries are frequently felt just above the medial and lateral epicondyles of the femur if the femoral artery is blocked. The descending genicular branch of the femoral artery can sometimes be felt. At the ankle the most frequent collateral pulse is the perforating branch of the peroneal artery.

It takes a great deal of practice and experience to become expert at palpating peripheral pulses but if allowance is made for normal variations it can be one of the most important parts of the examination of a patient suffering from peripheral vascular disease. It will be evident that a careful analysis of the major pulses and palpable collateral vessels enables the examiner to localise fairly accurately the site and the extent of an arterial block. It gives, however, only an imperfect estimate of the circulating blood flow and the potential capacity of the collateral vessels. In order to get a better idea of the blood flow to the limb for diagnostic and therapeutic purposes a number of special investigations may be performed.

R. B. L

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with the responses normally expected under the circumstances of the particular test.

METHODS OF DEFINITE VALUE

Tests of the capacity to dilate.—The practice of these tests remains the simplest to perform and the most informative of all the special methods Special or expensive equipment is not essential although in laboratories devoted to the study of peripheral vascular disorders such equipment is usually available.

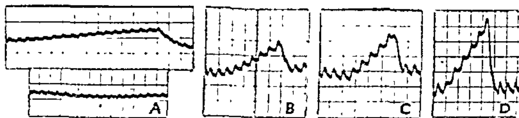


FIG. 94
The effect of indirect heating test upon toe pulse volumes and blood flows in a 48-year-old atherosclerotic with arteriographically proven femoral blocks A—before, B—25 minutes, C—35 minutes; D—40 minutes. There is an eleven-fold increase of blood flow (collecting cuff at ankle)

The rate of blood flow in a limb, or part of a limb, may be reduced because of organic disease of the vessels or because of a pathologically high state of vasomotor tone of the vessels. These can be simply separated by methods designed to release, directly or indirectly, vasoconstrictor tone in the limbs in question. Moreover, even though structural disease of the vessels is present it serves some purpose to ascertain the capacity of the collateral blood vessels to dilate and so to increase the blood supply to the tissues beyond the arterial block. A number of methods have been devised to release vasoconstrictor tone, the most effective of which are peripheral nerve block, indirect body heating and the injection of sympathetic blocking vasodilator agents. To measure the effects of these procedures alterations in skin temperature and digital plethysmography are the most useful and the simplest to interpret.

BODY HEATING was first performed by covering the torso of the patient with a heat cradle which contained from six to eight 100-watt bulbs.[25, 17] The subject and the cradle were then covered with blankets and heating was continued for sixty minutes. Indirect body heating* is more effective;[15] in it the hands are immersed in water baths kept at 113°F. for sixty minutes if the feet are being studied (Figs. 94 and 95), or the feet are immersed if the hands are the subject of enquiry. Both methods depend

* Indirect Body Heating is preferable to the term Reflex Body Heating since the latter refers to the prompt vasodilatation induced by stimulation of the sympathetic afferent nerves[4]

for their effect upon the integrity of the sympathetic nervous system and the return of heated blood from the warmed extremity to the general circulation where it can act upon the vasomotor centre. Thus no indirect vasodilatation occurs when the circulation to the limbs immersed in the water baths has been occluded Contrariwise no increase in blood flow occurs in limbs whose sympathetic nerve supply has been divided or whose vessels are too diseased to dilate.

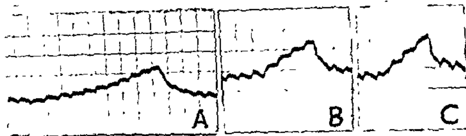


FIG. 95

The effect of indirect heating upon toe blood flows in a 46-year-old atherosclerotic with proven femoral artery thrombosis. A—before; B—20 minutes; C—40 minutes after beginning heating

The indirect vasodilatation methods have other limitations which must be mentioned and which make them less suitable than more local measures. Originally it was felt that thirty minutes of heating was sufficient to release vasoconstrictor tone but experience has shown that a number of subjects who have shown no response after that period show maximal dilatation if the heating is continued for sixty to ninety minutes.[5] Unfortunately such prolonged heating becomes unpleasant to the patient and may even, though rarely, be followed by some degree of collapse, particularly in the older subject In these older patients and in a limb the seat of advanced arterial obstruction the skin actually cools when indirect heating is performed The cardiovascular system in these circumstances seems unable even to maintain let alone to increase the blood flow in the ischaemic limb in the face of a generalised body vasodilatation There is in fact a reduction of blood flow in the affected limb—a variant of the borrowing-lending phenomenon—the blood from the diseased limb going to areas of vasodilatation elsewhere. It is considerations such as this which encourage our preference for measures that will release vasoconstrictor tone locally rather than generally.

PERIPHERAL NERVE BLOCK is one of the *most* [illegible] methods of [illegible] usually, a par [illegible] blocking the [illegible] produce a sig [illegible] blood flow to the region, if that is possible (Fig 96) By means of local nerve block the dilating effect is obtained in the limb in question and general haemodynamic alterations, which in themselves may nullify the test, are avoided.

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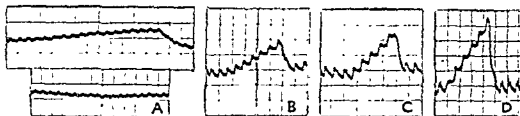


FIG. 94

The effect of indirect heating test
atherosclerotic with arteriographic
C—35 minutes; D—40 minutes

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* Indirect Body Heating is preferable to the term Reflex Body Heating since the latter refers to the prompt vasodilatation induced by stimulation of the sympathetic afferent nerves[4]

Seldom is any other nerve to the foot anaesthetised but the lateral popliteal nerve can be blocked where it lies superficially just below the head of the fibula. In the upper extremity a similar procedure is used to block the ulnar nerve as it lies behind the medial malleolus at the elbow (Fig. 97). The median nerve may be blocked as it lies under the tendon of the flexor carpi radialis at the wrist or just above the elbow as the nerve lies beside the brachial

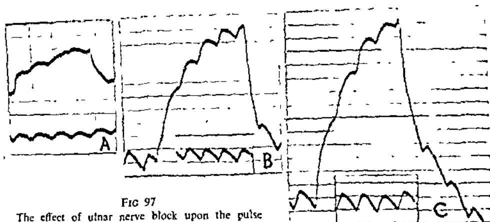


FIG 97
The effect of ulnar nerve block upon the pulse volume and blood flow through the fingertip of a 29-year-old woman with Raynaud's phenomenon; A—before, B—20 minutes; C—35 minutes after block; there is a three-fold increase of pulse volume and a five-fold increase of blood flow occluding cuff at wrist

artery It is rare indeed for a successful local nerve block to fail to produce an increase in local blood flow in the absence of advanced arterial obliteration. Thus if no rise in skin temperature or increase of pulse volume, and anaesthesia is present in the skin supply of the nerve blocked, it can be concluded that organic vascular disease exists and is of such a degree that sympathectomy will not produce any increase of local circulation.

VASODILATOR DRUGS have proved to be of definite value when nerve block may be inadvisable or inconvenient, if there is local infection in the foot, for example, or if it is desired to enclose the foot in a plethysmograph for simultaneous measurement of temperature and flow. As a reliable alternative to nerve block then, the intravenous injection of 50 - 75 mg. of Priscoline or preferably the intra-arterial injection of 50 mg. of the drug will be found to be satisfactory (Fig. 98).[18] The criticism of

...injection of Priscoline produces the ...effect in the affected limb and is painless and free from risk when a fine needle is used. As the injection is made the patient complains of a burning

The posterior tibial nerve is anaesthetised behind the medial malleolus where it lies beside the posterior tibial artery. A 1 per cent. solution of

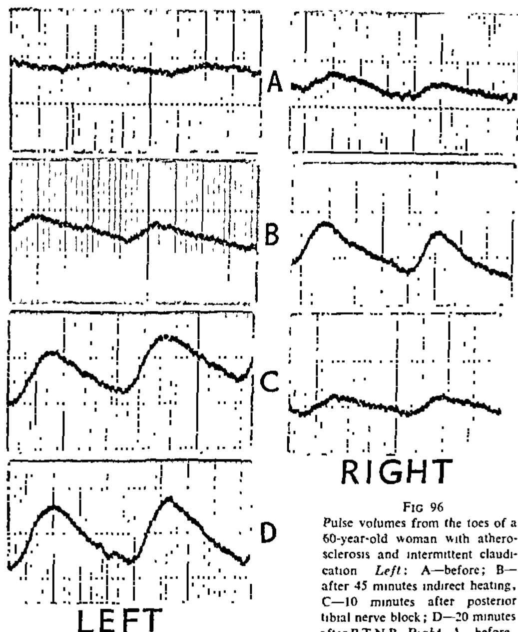


Fig 96

Pulse volumes from the toes of a 60-year-old woman with atherosclerosis and intermittent claudication *Left*: A—before; B—after 45 minutes indirect heating, C—10 minutes after posterior tibial nerve block; D—20 minutes after P T N B *Right* A—before, B—after 45 minutes indirect heating; C—demonstrates reflex vasoconstriction attending the *left* posterior nerve block This record demonstrates as well the occasional failure of indirect heating to produce complete vasodilatation

procaine is used to raise a skin wheal and the fine (hypodermic) needle is then advanced until paraesthesia running into the first toe is elicited, when an additional 3 ml. of local anaesthetic is injected. Within a few minutes a rise in skin temperature and blood flow will occur, if it is to be obtained at

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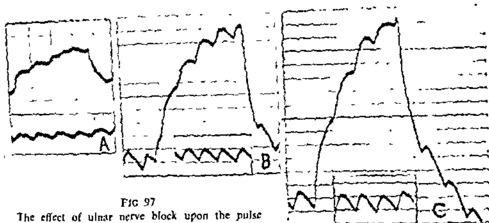


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The effect of ulnar nerve block upon the pulse volume and blood flow through the fingertip of a 29-year-old woman with Raynaud's phenomenon; A—before; B—20 minutes; C—35 minutes after block; there is a *three-fold increase* of pulse volume and a *five-fold increase of blood* flow occluding cuff at wrist.

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all (Fig. 96). Seldom is any other nerve to the foot anaesthetised but the lateral popliteal nerve can be blocked where it lies superficially just below the head of the fibula. In the upper extremity a similar procedure is used to block the ulnar nerve as it lies behind the medial condyle at the elbow (Fig. 97). The but also a peripheral blocking action which ensures completeness of response.

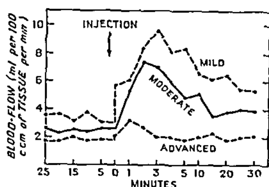


FIG. 98
Blood flow in feet of patients with mild, moderate and advanced arteriosclerosis after intravenous injection of *Priscol* 50 mg (*Lancet* 18)

The use of general or spinal anaesthesia in order to determine the adequacy and the potential of the peripheral and collateral circulations is rarely necessary. It is a useful expedient sometimes in a doubtful case to measure changes in the peripheral circulation when general anaesthesia is being employed for the purpose of performing arteriography. In such cases plethysmography is performed before and after the induction of anaesthesia and the degree of vasodilatation recorded. Generally speaking nerve block is simpler, safer and more reliable than any method in which generalised vasodilatation is produced. This criticism holds even more definitely for the injection of foreign proteins. Typhoid vaccine was formerly used intravenously to produce a vasodilatation but the febrile reaction is often severe and vascular thrombosis has been reported. The test is not now used.

Paravertebral block of the sympathetic ganglia in which the vasoconstrictor nerves to the affected limb run or synapse produces vasodilatation in that limb alone. It thus avoids the criticism of indirect body heating in that it does not produce generalised vasodilatation and it causes a release of tone in the whole limb rather than in just one part of it, as does isolated nerve block. Paravertebral block is, however, sufficiently difficult and uncomfortable to prevent its use as a routine laboratory procedure. If poorly performed it is diagnostically worthless and may be followed by distressing sequelae. Since adequate information can be obtained by simpler and more reliable methods paravertebral block is best reserved for use as a therapeutic measure.

SKIN TEMPERATURE is the simplest method for rough determination of slow changes in the rate of blood flow to a limb.[5, 7] Although skin thermometers can be used, a more reliable method employs thermocouples formed by the fusion of copper (or iron) and constantan filaments

Briefly, the method employs a single recording lead consisting of two thermocouples, one of which is kept at a known, constant temperature as by immersion in a thermos flask filled with water and the other is applied to the skin. When there is a difference in temperature between the two an

e.m.f. is generated and current flows through the wire connecting the two thermocouples. This current deflects a calibrated galvanometer the reading of which is added to or subtracted from the temperature of the water in the thermos bottle. Various modifications of this basic principle have been used and one of the latest and best is the automatically-recording potentiometer.[5] In this a measured current is passed through a calibrated slidewire resistor, providing a calibrated voltage drop across the slidewire. A portion of this current is opposed to the potential across the terminals of an iron and constantan thermocouple applied to the skin. The current flowing between the soldered metals of the thermocouple is proportional to the temperature at their junction, in short, to the temperature of the skin. The machine then amplifies the minute currents and records them on moving paper bearing a temperature scale. With this machine eight to twelve leads can be recorded in succession at thirty-second intervals

Under absolutely constant conditions skin temperature readings reflect fairly accurately the variations of blood flow in a limb but the time lag is great and sudden changes of blood flow can occur with little or no change of surface temperature Environmental conditions, thickness and quality of the skin and subcutaneous tissues, and particularly sudomotor activity influence skin temperature. In indirect heating the production of sweat on the part may lead to an altogether false reading. Moreover, as will be noted under plethysmography, there is a poor correlation between blood flow and skin temperatures. In fact skin temperatures may be almost maximal when the peripheral blood flow is below a value generally considered to be normal; conversely, a point may be reached beyond which the actual blood flow to the part may continue to increase, often substantially, with no further increase in skin temperature. It is a well-known fact that only a small part of the maximal blood flow is needed to warm the skin to significant vasodilatation levels. Finally, skin temperature readings are an index only of cutaneous circulation and give no information of what changes are occurring in the circulation through the muscles Nevertheless, if the limitations of skin temperatures are conceded they remain a simple and reasonably reliable index of the rate of blood flow in the part being studied.

Under usual laboratory conditions with an environmental temperature of about 70°F the surface temperature of the toes is, in general, at or near that of the room while that of the fingers is slightly higher When [illegible]
mental temperature is [illegible]
fully [illegible]
tion [illegible]
at wh[illegible]
dilatation [illegible]
and the la[illegible]
[illegible] tone. Thus a slow and incomplete [illegible] in skin temperature suggests an occlusive vascular disease rather than a vasospastic condition It must, however, be remembered that

under controlled conditions an increase of skin temperature of only a few degrees, after nerve block or other methods of vasomotor release, may be significant. After nerve block the temperature response is usually prompt but in the face of advanced ischaemia it may be necessary to wait as long as an hour before the maximum skin temperature is recorded. Thus a prompt increase of skin temperature to the full vasodilatation level indicates predominant vasospasm and predicts a good response to sympathetic denervation. The more delayed and the smaller the increase in skin temperature the more likely is it that the condition is due to organic disease and so less satisfactory for surgery.

In methods employing generalised vasodilatation a rise in body temperature occurs. This was particularly true when typhoid vaccine was employed. The " vasomotor index " had then to be calculated by dividing the difference between the rise in skin temperature and the rise in mouth temperature. A " vasomotor index " of 1·5 or more implied a suitable candidate for sympathectomy. This calculation is seldom used now and is of little practical or prognostic value. The response of the skin temperature to local or general methods of vasomotor release must be carefully studied against the background of the individual clinical findings and the examiner's familiarity with the limitations of the methods employed. If such analysis is applied the method will prove to be of practical value in differentiating organic from vasospastic arterial disease and to aid in prognostication of the benefit to be gained from surgery.

Temperature readings in the subcutaneous tissues and the muscles show a gradient of rising temperature—the deeper the tissue the higher the temperature—although the change is usually one of only 1° C. or so. Generally speaking, the changes in subcutaneous temperature run parallel to those in the skin although they are of much smaller magnitude. Measurements of subcutaneous temperature are of little or no clinical value.

PLETHYSMOGRAPHY used to be relegated to the field of physiology and research and was considered too complicated for practical laboratory use.[1] This may have been true in the past but it is no longer so now that several accurate and simple digital plethysmographs have been devised and perfected.[21, 32] Plethysmography has a wide range and a quick response and is therefore preferable to the skin temperature method of recording peripheral blood flows mentioned above. Details of the principles, practice and limitations of venous occlusion plethysmography, the digital pulse volumes and the relationship between the two are discussed in the appendix at the end of this chapter.

Venous occlusion plethysmography may be performed, or more simply the amplitude of the pulse volume may be measured and taken to indicate the state of the blood flow to the part. The latter is a simple clinical method and obviates some of the difficulties and criticisms inherent in the method of venous occlusion plethysmography. The relationship between absolute blood

flows as measured by venous occlusion plethymography on the one hand, and the pulse volume on the other, is fairly linear over the greater part of the range of blood flows from complete vasoconstriction to maximal dilatation so long as the part being studied is kept at or slightly above the heart level.[21, 3] For clinical purposes digital pulse volumes are a simply obtained, accurate and practical method of estimating the rate of blood flow through

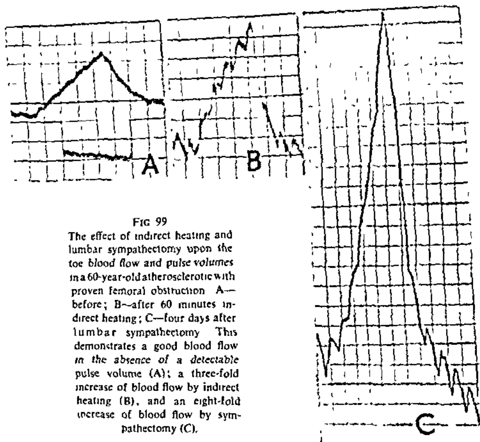


FIG 99
The effect of indirect heating and lumbar sympathectomy upon the toe blood flow and pulse volumes in a 60-year-old atherosclerotic with proven femoral obstruction A—before; B—after 60 minutes indirect heating; C—four days after lumbar sympathectomy This demonstrates a good blood flow *in the absence of a detectable* pulse volume (A); a three-fold increase of blood flow by indirect heating (B), and an eight-fold increase of blood flow by sympathectomy (C).

a digit—the part of the body in which peripheral vascular disorders exert their greatest effects. It is true that in some patients with severe organic occlusion or intense vasospasm a pulse volume cannot be recorded, yet venous occlusion may demonsrate that blood is flowing through the part but at too low a pressure to produce a measurable pulse volume (Fig. 99). Such cases are rare and do not detract from the clinical importance of the test.

Vasodilatation having been induced by one of the methods mentioned, the capacity of the vessels to dilate, as reflected in the increased rate of blood flow through them, is measured by an increase in the amplitude of the pulse volume or by an increasing steepness of the collection curve if venous occlusion

plethysmography is being employed. The rapidity of development of this increase and its approximation to the maximum flow levels known to be normal allow one to assess the extent of vasospasm, the degree of organic disease and the potential of the collateral circulation. An increase of 100 per cent. above the maximum value of pulse volume or blood flow obtained in the equilibrium period before the test was applied is the least response which can be considered as significant. As with any test, the change observed must be considered against and integrated with the clinical facts before it can be used as a yardstick for treatment or prognosis.

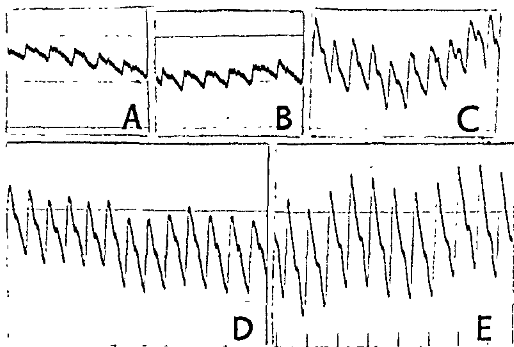


FIG. 100

Indirect heating test upon a 34-year-old man with recurrent Raynaud's attacks nine months after left cervico-dorsal sympathectomy *Left:* A—before, B—20 minutes, C—40 minutes, and D—60 minutes after heating *Right:* E—60 minutes after heating in the non-sympathectomised hand. This demonstrates marked sympathetic activity in the left hand which should have shown no change if sympathetic denervation had been complete.

Before leaving this group of tests it should be made apparent that they are also useful in assessing the completeness of denervation after sympathectomy (Fig. 100). All the tests described depend upon the integrity of the sympathetic nervous system at some point in the reflex arc Thus if a technically successful indirect heating test or nerve block fails to increase the skin temperature, pulse volume or absolute blood flow after sympathectomy when it increased them before it, it can be assumed that sympathetic denervation is complete, unless arterial disease has advanced to the point of complete occlusion in the interim.

In summing up this group of tests of potential vasodilatation it is our experience that indirect body heating by the immersion method, and peripheral nerve block, are simple, safe and reliable methods of producing release of vasomotor tone in a limb, and that digital pulse volume alterations are more reliable than skin temperature changes as an index of an increase in the rate of blood flow, and therefore of vasodilatation, in the part under study. Venous occlusion plethysmography gives absolute values and is accurate but it is perhaps too time-consuming for routine clinical investigation. Its primary application is in the scientific study of the physiology of the peripheral circulation. All these procedures have definite limitations which must be remembered. The greatest limitation of this group of tests is their inability to delineate the site and extent of the block in the involved vessel and for this information further tests must be employed.

Arteriography.—Roentgenological visualisation of the peripheral arteries after the intra-arterial injection of radiopaque dye affords information that can be gained by no other method. It enables the site, the extent and, in some degree, the nature of an arterial block to be ascertained. It also provides information about the natural compensations that have developed in the limb and of the state of the vessels beyond the area of arterial obliteration. The need for such data is becoming increasingly important now that surgical intervention is being directed to the obliterated arterial [illegible] [illegible]

[illegible] information is necessary and when it cannot be obtained by the more usual measures. The technique and application of arteriography are discussed in detail in Chapter VI

METHODS OF LIMITED VALUE

Ergometry.—A more objective evaluation [illegible] tion in an [illegible] far he can [illegible] when it is [illegible] limb is the seat of an intermittent claudication which is masked by the more advanced disease in the presenting limb More especially in attempting to evaluate the efficacy of various forms of treatment upon intermittent claudication an accurate and objective test must be used It is in such circumstances that controlled walking or controlled exercise is essential. The former is most useful in unilateral disease whilst the latter is best applied when the arterial occlusion is bilateral.

A treadmill, or "claudicometer," is a moving platform which can be made to move at a variety of speeds which are constant and reproducible. By this method a quite accurate estimate of the "claudication distance" can be obtained Ergometry is a less expensive and a simpler method of obtaining

accurate objective information of the capacity of the muscles to perform work. It is applied by having the patient voluntarily contract the calf muscles against the resistance of springs, weights or progressively increasing pressure. Both methods, treadmill and ergometry, are sufficiently discriminative to be valuable indices of the functional efficiency of the arterial circulation in the limbs being studied. The major criticisms of such methods are the difficulty of assessing the effect of will on the performance and, in ergometry, of making sure that muscle groups other than those under study are not contributing to the total effort. In spite of these and other faults, the methods are more valuable than the patient's statements as to his "claudication distance" and the effects of treatment upon it.

A number of ergometers have been constructed.[5, 31, 33, 12] A convenient type consists of two uprights bolted to a platform upon which the patient sits in an ordinary chair. His femur is slightly flexed at the hip and his leg is parallel to the uprights. Suspended from the uprights are two cross bars, one fixed and the other suspended from it by two springs. The moveable one is approximated to the fixed one by raising the heel from the floor. This movement compresses a bulb. Air is forced from the bulb and this activates a pen on a float recorder whose excursion is recorded on a kymograph. The exercise is regulated at forty per minute by a metronome and a full excursion is ensured by having the patient make an electric contact which switches on a light only if the bulb is completely compressed. With this ergometer only the calf muscles are exercised, no special training is necessary and repeated performances by the same individual produce consistently similar results. Although such instruments are seldom used they find their greatest field of application in revealing bilateral disease and in assessing, objectively, the effects of drugs and surgery upon intermittent claudication

Oscillometry.—This is a mechanical method of measuring the changes produced in the volume of a limb by the arterial pulsations.[2] As currently performed it is little more valuable than is palpation of the peripheral pulses by the finger tips except that it gives an objective record for the purposes of comparison and future reference. The instrument is impossible to calibrate and its sensitivity is low. It gives no indication of blood flow. Sometimes, even if the collateral circulation is more than adequate, oscillometry shows no pulsations; the weak expansile force characteristic of collateral circulation may be inadequate to overcome the cuff pressure. Finally, the range of normal values is so wide that it can be said that there are really no consistent normal values. In our hands the oscillometer has been of little or no practical value and it is not now employed. Recording oscillometers are available and although they remove the personal equation they are not only expensive but subject to the same criticisms as the standard Pachon type.[8]

Briefly, the technique consists of wrapping a pneumatic cuff snugly around a limb at various levels, *i.e.* ankle, calf, thigh. The cuff is connected to a rigid, hermetically sealed box inside which is an aneroid capsule upon which

is a delicate needle. The box, the aneroid and the cuff are all connected to each other. Air is pumped into the chamber, the cuff pressure is inflated to above systolic blood pressure and then deflated by steps of 10 to 20 mm. of Hg at a time until excursion of the needle on the aneroid is no longer evident. The level for optimum readings is between 120 and 80 mm. of Hg. The maximum oscillation of the needle is known as the "oscillometric index." In the arm this varies between 4 and 20 and in the leg between 3 and 12 in the presence of a normal circulation. These normal values are clearly so widely variable that the method can only be considered as a gross test of pulsatile blood flow. It does not register the collateral circulation and in fact is less valuable than a carefully performed physical examination of the limb.

Fluorescein circulation test.—There are numerous tests available for estimating the speed of the circulation between two parts of the body, *e.g.* sodium cyanide, decholin, and magnesium sulphate. Most of these agents are used for detecting the presence of heart failure and particularly the state of the pulmonary circulation. The best test applicable to the peripheral circulation is the fluorescein circulation time.[16, 19] Tests using radioactive isotopes are being investigated but their value has not yet been established. The principle of the test is that after the injection of fluorescein the normally vascularised skin becomes fluorescent under ultra-violet light illumination. A similar test has been used to determine the adequacy of the intestinal blood supply in a strangulated loop of bowel. In the peripheral circulation the normal fluorescein times show such a wide scatter that only gross assumptions can be drawn from the method. As in all such methods the end-point depends upon the arrival of a "detectable" quantity of the agent used so that the circulation times are usually underestimated.

The test is performed by raising histamine wheals on the dorsal aspects of the feet, below each knee and on the left antecubital fossa at the end of a period of indirect body heating. Four ml of 20 per cent. sodium fluorescein and 2 per cent. sodium bicarbonate is rapidly injected into a median cubital vein whilst one of the team handles a stop watch and observes the wheals under an ultra-violet light. As the blood carrying the fluorescein reaches the wheal a greenish-yellow glow develops. This is the end-point and the time is noted. The time for the fluorescein to reach the left antecubital fossa is assumed to be the circulation time through the right heart, lungs and the left heart and this is subtracted from the leg and foot values. The intrathoracic value is about nine seconds and the corrected time to the feet is normally eight to thirteen seconds. The test has little practical value although differences in time between two limbs under similar conditions is [illegible] test has never [illegible] employ it sinc[illegible]

Venograp[illegible] [illegible] less satisfactory than arteriography and any conclusions drawn from the pictures obtained must be inter-

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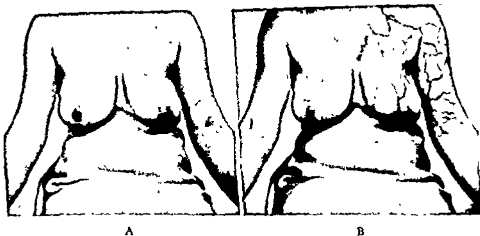
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venous blood from the affected limb can be compared to that from the normal limb of the same individual under the same circumstances. The venous and the arterial blood are collected from both limbs without a tourniquet and [illegible] method of Van Slyke. [illegible] : an oxygen [illegible] content approaching that of the arterial blood [illegible] ous fistula is present.

METHODS OF DOUBTFUL VALUE

Infra-red photography.—This technique will seldom demonstrate distended superficial veins that cannot be detected clinically but it affords a permanent, objective record of unilateral differences in the superficial veins which would not have been reproducible by ordinary photographic methods. Infra-red photography relies on the fact that blue is a colour to which infra-red



A B

FIG 102

(A) Plain and (B) infra-red photograph to demonstrate the collateral venous circulation after spontaneous thrombosis of the left axillary vein.

plates are more sensitive than ordinary photographic plates. Thus a superficial vein distended with blood shows up vividly and the photograph provides a permanent record of the venous pattern (Fig. 102A and B).

Intradermal wheal tests are performed by injecting, intradermally, either 0·1 cc of 1 : 1,000 histamine phosphate[35] or 0·2 ml. of 0·85 per cent. sodium chloride[20, 36] at regular intervals in the limb in question, *e.g.* base of great toe, dorsum of foot, ankle, mid leg, above the knee and mid thigh. After intradermal histamine a wheal normally develops within ten minutes. It is assumed that the rate of development of the wheal is directly proportional to the rate of cutaneous blood flow. A delay in the development of the wheal

preted with the greatest reserve (Fig 101). Its limitations became apparent when it was attempted to apply the method as an index of the patency and valvular function of the deep veins of the leg in the post-phlebitic state. The valvular pattern in the deep veins of the normal limb is highly variable and this makes comparison between different individuals and even opposite limbs of the same individual unreliable.[20] The examination has no especial value in the acute stage of thrombophlebitis where it has been shown that in at least 30 per cent. of cases a negative phlebogram is obtained in the presence of thrombosis and we rarely find it necessary to perform venography to establish the diagnosis of the post-thrombophlebitic syndrome in the lower extremities. In the upper limbs the procedure is rarely performed and then only to demonstrate an axillary or superior vena cava obstruction. The test is discussed in detail in Chapter VI.



Fig. 101
Normal venogram done by the retrograde method

Arteriovenous oxygen differences.—It has been stated that an obvious criterion for evaluating the adequacy or deficiency of the circulation is the arteriovenous difference in oxygen content of the blood. The rationale of this is that the more rapid the blood flow the less time there is for gaseous exchange to occur in the tissues and the more closely does the oxygen content of the venous blood approach that in the arterial blood. This is not a valid assumption because of the inability to control even the more obvious variables such as environmental temperature, individual reaction to the sensory stimulation, the degree of mixing of muscle and skin blood in the samples drawn and, in the case of the hands and feet, the action of arterio-venous shunts. Work from this laboratory shows that the range of variation of oxygen content of venous blood from normal individuals is so wide that comparison between normal values and those obtained from individuals with peripheral vascular disorders is quite unreliable. The only place where arterio-venous oxygen differences are useful is in the presence of an arterio-venous fistula where the

Venous pressure may be measured quite accurately by direct venipuncture and water manometry. In most laboratories now a variety of transducers is available for such measurements. These include strain gauges and capacitance manometers, and the latter are used in this laboratory. After suitable that a permanent record is obtained.

Sweat secretion.—Sweating tests are of interest mainly from two points of view, first to assess the completeness of sympathetic denervation and secondly to map out the anatomical areas of the skin surface denervated by a particular operation[28, 29] or nerve lesion.[10] Although there is some suggestion that the activity of sweat glands varies in different types of vascular disorders there is as yet no satisfactory method of obtaining standardised results of comparative value Nor is there any standardised method of producing sweating Only in hyperhidrosis, where the clinical picture seldom needs any amplification, are tests of sweating of any clinical value in differential diagnosis.

Sweating may be produced by the application of heat to the body or by the exhibition of drugs. In the former a hot drink and 5 grains of aspirin are given and a heat cradle, as for indirect vasodilatation, is applied; within thirty minutes the parts capable of sweating become damp. Drugs may be used but are sometimes accompanied by unpleasant side reactions which have to be controlled by atropine. The usual drugs given are pilocarpine hydrochloride 6 to 13 mg subcutaneously or, preferably, furmethide 5 mg. which is equally effective and almost devoid of side effects[9] These drugs produce sweating by stimulation of the nerve endings to the sweat glands which are anatomically sympathetic but pharmacologically cholinergic To outline the extent of the area of sweating colorimetric or electric methods are used.

The colorimetric evidence of sweating depends upon the presence of moisture completing a chemical reaction which produces a colour or a colour change A number of powders and solutions are available the most [illegible] of which are the [illegible]
(2 6 gm [illegible]
bicarbona[illegible] cobaltous chloride in alcohol[30] which turns from blue to pink (saturated solution of cobaltous chloride in alcohol) and the iodine-starch test of Minor[22] in which an ivory coloured powder becomes deep blue (1·52 gm of chemically pure iodine, 10 ml. of castor oil and absolute alcohol to 100 ml.; paint on and when dry dust with fine rice starch) The colorimetric method is necessary when a photograph is desired; it is a rather untidy procedure (Fig 103).

The most sensitive and simplest method of determining areas of reduced sweat secretion depends on the capacity of the skin to act as a conductor of a minute electric current.[27, 28] Skin is a poor conductor when dry but when it is moist it becomes a good conductor. Thus the presence or absence of sweating can be recorded by directly reading the skin resistance in ohms when a one-volt direct electric current is passed Two electrodes are used, an

(and the flare) implies reduced skin circulation. When intradermal saline is used it is injected until a wheal is produced, the time for complete disappearance of which is compared with the normal of sixty minutes In the presence of oedema, regardless of the etiology, absorption is very rapid, being proportional to the degree of oedema. When ischaemia is present the wheal also rapidly disappears—less than ten minutes indicates severe ischamia or imminent gangrene. The rationale of this test is that in the presence of impaired circulation there is disturbed water balance in the limbs, *i.e.* an increased affinity of the tissues for water causing rapid disappearance of the wheal.

Neither test gives information that cannot be obtained by simpler and more reliable means so that there is little to merit their continued use.

Tests of clotting tendency.—A number of tests have been described purporting to predict an increased clotting tendency in the blood so that patients susceptible to venous thrombosis may be recognised and given timely anticoagulant therapy. These will not be discussed since it is felt that none of the tests is sufficiently accurate or consistent in its predictions to be of practical value for clinical use. To be valuable such a test must be simple enough to perform at the bedside, and consistently accurate. There is no test yet which fulfils these simple clinical criteria.

Tests of capillary fragility, whilst of value in the diagnosis of purpura or other haemorrhagic diathesis, have little application to the clinical study of peripheral vascular disorders

METHODS OF PHYSIOLOGICAL INTEREST

Venous pressures.—Unless absolute values of venous pressure are wanted for some purpose their estimation by other than clinical means is seldom indicated. Thus if distension of a superficial vein persists when the limb is raised above heart level it may be assumed that some degree of venous obstruction is present. In most situations the venous pressure is that of the hydrostatic pressure of a column of blood from the level of the right auricle to the part being examined. In such a case where venous distension persists on elevation above the heart the level at which collapse finally occurs may be taken as the venous pressure.

In both the superficial and deep veins of the leg the resting venous pressure is that of the hydrostatic column of blood to the right auricle. When exercise begins the venous pressure falls in the superficial veins if the deep veins are competent but in the presence of deep venous incompetency the pressure rises.[6, 38] Such a situation exists in the post-thrombophlebitic state and similar elevations of venous pressure occur at rest in the presence of congestive heart failure, cardiac tamponade and arterio-venous fistulae It is seldom necessary to resort to absolute measurement for diagnosis unless a numerical record is desired for future reference.

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are undertaken valuable information about the capillary morphology in vascular diseases may be obtained. Most of the studies that have been performed have been upon the capillaries in the nail folds of the fingers and there are practically no data available in the toes.

There is a great variation in the capillary pattern in the normal limb but the capillaries are usually arranged in rows of loops and the blood can be seen streaming through them.[14] The flow of blood is periodically interrupted by clear spaces which are felt to be columns of plasma. Variations on this theme are noted in vascular disease.[40] In Raynaud's disease the capillary loops are few and incompletely filled and the flow is static in the stage of syncope while in the cyanotic phase the loops are numerous, dilated and the flow is sluggish In Buerger's disease the loops may appear constricted and few in number or numerous and dilated, with slow, irregular flow. It may be said that, at present, there is no morphological appearance characteristic of a definite disease process so that as a practical procedure in clinical practice its applications are few. A more concerted study of the capillaries may well yield information of great value to the physiologist as it appears to be doing in the work on capillary flow and morphology in various clinical states.

The procedure requires an intense light source for taking the pictures and a lesser source for searching the fields. The illumination must not heat the tissues or abnormal changes will occur. The nail folds of the fingers and toes are examined through an oil immersion lens under cedar oil after the digit has been gently washed. Scraping, scrubbing or other methods of cleansing the skin must not be used as they will produce changes in themselves. When the field to be studied has been localised with the searching light, automatic releases expose the field to an intense light of very short duration and to 35 mm film upon which the field is permanently recorded. The procedure is relatively simple but quite time-consuming and it is doubtful whether it is, at the present time, of more than academic interest.

Calorimetry.—This is an indirect method of determining the blood flow through an extremity which depends upon the rate of transfer of heat from the part being studied to water in which it is immersed. Although the method is free from some of the obvious objections of venous occlusion plethysmography, it is more complicated, equally indirect and no more [illegible] techniques are available to give the same [illegible] method is its inability to measure sudden ch[illegible] recent modifications of the method by Greer[illegible] alone, are encouraging From the stanc[illegible] temperature [illegible] calorimetry. [illegible] of its principl[illegible]

Radioactive isotopes.—Activated sodium, globulin and albumin have been employed in the study of peripheral vascular diseases[23, 37, 13] Radioactive

* *J. Appl. Physiol.* (1951), 4, 37

indifferent electrode placed anywhere on the body and an examining electrode which is used to map out the area in question. The readings may be as low as 100,000 ohms in the normally sweating skin or as high as several million ohms in anidrosis. The method is simple, clean and sensitive but it cannot be photographed and it possesses inherent technical difficulties which are as important to the result as are the properties of the skin itself. The chief difficulties are polarisation which is inevitable with a direct current,

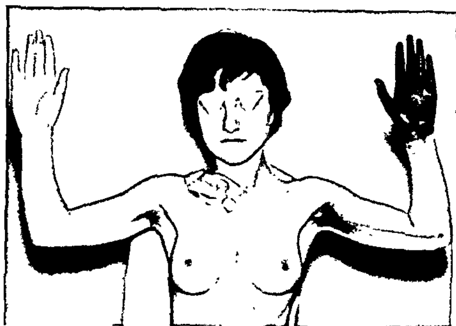


Fig. 103
Colorimetric (quinizarin) sweating test to show the effect of right cervico-dorsal sympathectomy on primary hyperidrosis

the variation of resistance with the size of the area of contact between the electrode and the skin, and the infinite care needed to be sure that no moisture is carried on the electrode from one part explored to another. Until there is an accurate method of measuring sudomotor activity quantitatively the examination will be used chiefly to confirm the extent and completeness of sympathetic denervation in areas where plethysmography is impractical and skin temperature changes are small, *i.e.* head, trunk, thighs. The skin resistance method is more convenient than the colorimetric methods unless a photographic record is desired.

Capillary microscopy.—Studies of the nailfold capillaries in man have been infrequent, the normal morphology is only roughly known and the practical value of the procedure is limited.[14] The method permits examination of only a particularly minute portion of the capillary circulation; it cannot be assumed that the changes seen in the nailfold studied are uniformly present throughout the capillary bed. It is possible that when more detailed studies

The *process* is *not* one of *thrombosis* because it can be reversed by warmth in vitro and in vivo. Only if the ischaemia produced by the blockage of the vessels *by the agglomerated cells persists* for a sufficient length of time may necrosis and loss of tissue result. A high titre is a rare finding in the subject of peripheral vascular disease and determination of cold haemagglutinin titre is of little practical value (see p. 510).

Similar conditions apply to the cryoglobulins which may also develop in generalised diseases much as cold agglutinins do and are exposed by a degree of cold which reduces the blood temperature to as little as 37°C., but usually less. *Warming* to above 37°C. generally causes *release of the* agglomerated red cells enmeshed in the precipitate of cryoglobulin. Should the period of vascular obstruction persist for long periods, tissue loss or even gangrene may occur but very rarely.

R. B. L.

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Autonomic Nervous

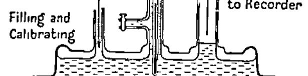
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sodium has been used in two ways in an attempt to assess the rate of blood flow in a part. First, it has been injected into skin, subcutaneous tissues and muscle and the rate of its disappearance has been measured. The rate of disappearance has been assumed to be proportional to the rate of blood flow. Secondly, radioactive sodium has been injected intravenously and the time of arrival at some point in the body has been measured—in other words a circulation time. Although this substance gives some qualitative evidence of the state of the circulation it gives no quantitative information. Moreover, the disappearance rate does not reflect the rate of blood flow through arterio-venous anastomoses but only that through the capillary beds. As yet the method is too impractical and further controlled studies are necessary before it can be considered useful.

Activated proteins, globulin and albumin, have been applied chiefly to the study of oedema of the extremities. The disconcerting feature of such studies is that the speed of appearance of these substances at the groin when injected intravenously, or their rate of disappearance locally when injected subcutaneously into an oedematous foot, is approximately the same as in the normal.[13] As yet radioactive proteins have added little or nothing to our understanding of chronic oedema and this causes some concern over the current concepts of oedema formation. In the oedematous limb at least these complex proteins are capable of passing rapidly through vessel walls into the general circulation whereas it was formerly felt that their structure and size prevented this. It is possible that tagged elements are going to alter many of our concepts of the peripheral circulation and lymphatic function but so far they must be considered as biophysical methods needing extensive further study. They are not yet clinically applicable.

Cold haemagglutinins and cryoglobulins.—An antigen-antibody reaction between human erythrocytes and serum in which haemagglutination is observed only at low temperatures is found regularly in certain diseases and sporadically in others. Their presence usually cause no signs or symptoms though occasionally it is associated with cyanosis or haemolytic anaemia. In rare instances gangrene of the tips of the extremities occurs[24] and no pathological abnormality other than a relatively high titre of cold haemagglutinins can be demonstrated Of the many people who have a high titre few ever have symptoms of arterial insufficiency.

Patients with a high cold haemagglutinin titre may be normal in all other respects, presenting neither cause for the high titre nor any effects from it. The titre may be high, however, in severe anaemias, transfusion reactions, acute or chonic infective conditions and high titres have been reported also in Raynaud's phenomenon, leukaemia, tuberculosis and many other diseases. Clumping of the cells occurs on exposure to cold and is reversed by warming to body temperature. The fault lies in the serum, not in the red cells, since the serum will agglutinate the red cells of other individuals whereas the red cells of the susceptible patients are not agglutinated by the serum of others.



ARM

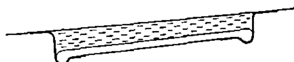


FIG. 105
Lewis and Grant's plethysmograph for the forearm.
(*Barcroft and Swan—Sympathetic Control of Human Blood Vessels.*)

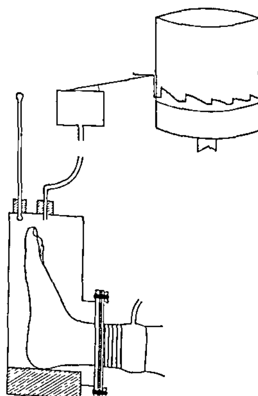


FIG 106
Diagram of the foot in the plethysmograph, showing method of making an air-tight joint at the ankle. Also the float recorder needle and tracing on drum and the venous occlusion cuff.
(*St Thomas's Hospital Reports.*)

PLETHYSMOGRAPHY

Although apparatus for determining changes in the volume of an organ was in use as early as the seventeenth century,[14] it was not until 1905 that the principle of plethysmography was used to determine the rate of blood flow through an organ, in this case the kidney, by Brodie and Russell.[4] From their descriptions it is probable that they utilised the technique for determining the blood flow in limbs since they say: " It is also applicable to a limb for

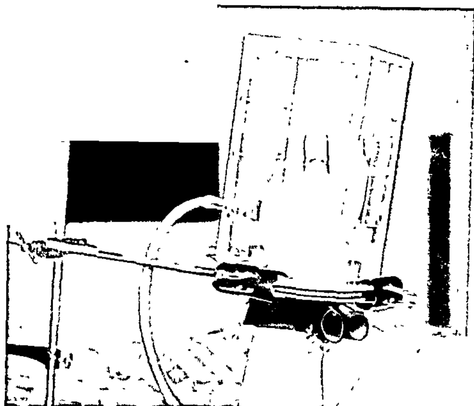


FIG. 104
Illustration of a hand in the plethymograph The venous occlusion cuff can be seen on the wrist (*St Thomas's Hospital Reports*)

the venous outflow can be blocked there by a circular ligature with so much force as to compress the veins without interfering with the arterial inflow." These observations were placed on a firm foundation, and the principle utilised to determine blood flow in the upper limb of man four years later by Hewlett and van Zwaluwenburg.[13] The latter authors enclosed the hand, forearm and elbow in their instrument. Since then numerous improvements have been made, so that now only part of the limb is placed in the plethysmograph and water is used to maintain a more constant environment around the limb and to facilitate rapid conduction of volume changes. Too, it has been shown that the hand and foot plethysmograph measures predominantly circulation through skin and, in the cool subject, the calf and forearm plethysmograph

graphs are so designed as to accommodate only that part of the finger beyond the distal interphalangeal joint since more proximal parts of the digits consist chiefly of bone and tendon. The plethysmograph is sealed to the digit with

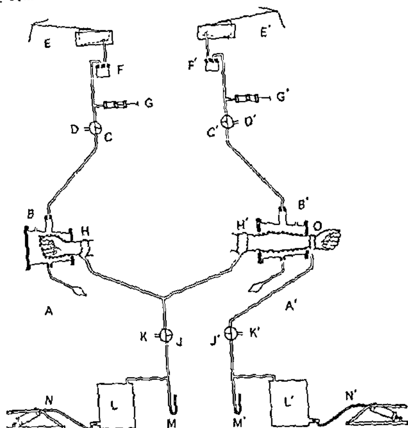


FIG. 108

Diagram of apparatus for recording the rate of arterial inflow into the right hand and left forearm. AA'—plethysmographs (thermometers not shown); BB'—vertical glass tubes, C C'—three-way glass ... side tubes com- ... G G'—syringes; ... side tubes com- ... M M'—mercury ...

(... —Sympathetic Control of Human Blood Vessels.)

a putty-like substance called "Sealastik" and connected to the recording transducer by pressure tubing Air conduction is used throughout since the usual objections to air are of minor importance in such a small volume system (see below on use of air or water conduction).

The fitting of a hand and forearm plethysmograph to the subject will be described in some detail and will apply with little alteration to the foot and calf. The hand is slipped into a rubber surgical glove, several sizes too large, which has been stuck round the wrist to the edge of a hole, shaped to

measures mainly blood flow through skeletal muscles. Finally, since it is the most peripheral part of an extremity, namely the digits, in which both vasospastic and occlusive vascular diseases play the greatest havoc, a desire for knowledge of the circulatory changes in the fingers and toes has led to the development of a number of sensitive digital plethysmographs for the study of those parts alone.[5, 6, 12, 17, 19, 21]

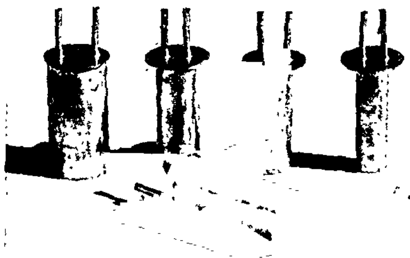


FIG. 107
Phosphorbronze finger-tip plethysmographs.

Plethysmographs.—The plethysmograph in which the part of the limb to be studied is placed is a rigid air and water-tight container constructed of metal (copper, aluminium) or plastic (Perspex). The use of transparent plastic permits the enclosed limb to be observed during the procedure and any abnormal changes, *e.g.* venous congestion, can be noted and corrected. A simple form of hand plethysmograph is shown in Figure 104; a forearm or calf plethysmograph in Figure 105; and a foot plethysmograph in Figure 106. The advantage of metal in the construction of the plethysmographs is that the exterior may be heated with a small flame to keep the temperature of the water within at the required level. If plastic is used a built-in thermostatically controlled heater (as used in small tropical fish aquariums) is a satisfactory method of keeping the water temperature constant, but on the other hand such a unit is more bulky and there is a danger of electrocution. Recently a simple temperature controlled plethysmograph has been described which seems to be free of such a hazard.[11]

For the fingers and toes a series of light metal cylinders of varying sizes are used (Fig. 107). The use of malleable phosphorbronze enables the plethysmograph to be moulded somewhat to the shape of the digit There are two ports from the end, one for conduction to the transducer and the other for calibration by means of a microsyringe. The digital plethysmo-

graphs are so designed as to accommodate only that part of the finger beyond the distal interphalangeal joint since more proximal parts of the digits consist chiefly of bone and tendon. The plethysmograph is sealed to the digit with

FIG 108

Diagram of [illegible]
and [illegible]
ver[illegible]
mu[illegible] recorders; F F'—traps, G G'—*syringes;* H H' O—*pneumatic cuffs;* J J'—three-way glass taps; K K'—side tubes communicating with room air; L L'—reservoirs of compressed air; M M'—mercury manometers; N N'—foot pumps.

(Barcroft and Swan—Sympathetic Control of Human Blood Vessels)

a putty-like substance called "Sealastik" and connected to the recording transducer by pressure tubing. Air conduction is used throughout since the usual objections to air are of minor importance in such a small volume system (see below on use of air or water conduction).

The fitting of a hand and forearm plethysmograph to the subject will be described in some detail and will apply with little alteration to the foot and calf. The hand is slipped into a rubber surgical glove, several sizes too large, which has been stuck round the wrist to the edge of a hole, shaped to



FIG. 109
Illustration showing plethysmographs on the right hand and the left forearm
(Barcroft and Swan—Sympathetic Control of Human Blood Vessels)



FIG. 110
Illustration of the apparatus being used to determine the blood flow in the foot
(St Thomas s Hospital Reports)

fit the wrist, in a ¼" thick rubber diaphragm. A selection of diaphragms is kept with holes of varying size and shape for various sizes and portions of the extremity The diaphragm fits the wrist snugly, but not tightly, for venous congestion must be avoided. By means of two semi-circular metal plates the periphery of the diaphragm is bolted by wing nuts firmly to a 2" wide flange on the end of the plethysmograph which is filled with water at 32°C up to the lower part of the vertical glass tube. The weight of the water presses the glove against the hand. The plethysmograph is mounted on a retort stand placed on a small table beside the subject. Its height is slightly above the level of the heart to ensure venous drainage, and the elbow is bent slightly to minimise the communication of respiratory movements to the hand. The same principle holds for the foot where a soft, loose, latex rubber sock can be used or the foot placed directly in the water while a rubber cuff is sealed to the skin of the ankle with rubber cement. The use of a rubber glove or sock obviates the necessity of cementing the rubber cuff to the skin and also prevents the possible ill-effects of maceration to an ischaemic limb.

For the forearm (and calf) a loose sleeve of thin latex rubber fixed at each end round a suitably shaped central hole in a rubber diaphragm is slipped over the upper part of the forearm or calf. The rubber diaphragms are bolted to both ends of the plethysmograph by wing nuts and metal plates. The temperature of the water is kept at 34-35°C.[2] The recording apparatus and the positions and arrangements for inflating the cuffs for a hand and a forearm are shown diagrammatically in Figure 108 and in place in Figure 109

Recording system.—The most practical method of recording blood flows from the hand, foot, forearm and calf is by the use of a float recorder activating an ink-writing pen which is applied to glazed paper on a continuous paper multi-speed portable kymograph (Fig. 110). In the laboratory a similar system may be used or a fixed bench kymograph using smoked paper is equally satisfactory and is unsurpassed for obtaining attractive records Calibration is done by injecting a known quantity of water into the plethysmograph with the extremity in place so that the calibration is obtained under the same conditions as the blood flow measurements.

For digital plethysmography the movement of a sensitive galvanometer is photographed on a multi-speed camera. Although direct writing digital plethysmographs are available[21] the amplification necessary to drive a pen recorder and the cost of the equipment is considerable, whereas the digital plethysmograph in use in this laboratory is inexpensive, durable and sensitive.[17] The R C A. transducer tube (No. 5734) can also be attached to the hand or calf plethysmograph as shown in Figure 111. The disadvantages of camera recording are several First, it is costly compared to kymograph paper and that used for other direct writers. Secondly, the record is not immediately available for examination as the experiment progresses and

occasionally, even in the best-ordered societies, the photographic paper runs out or does not come through. Finally it is difficult, unless an oscilloscope is available for monitoring the blood flows, to detect and to correct artefacts (infra).

Use of water or air conduction.—The major objection to air conduction is the large coefficient of expansion of air so that a small temperature change, as produced by heat given off from the enclosed extremity, *may* produce a considerable increase in the volume of air within the plethysmograph. This

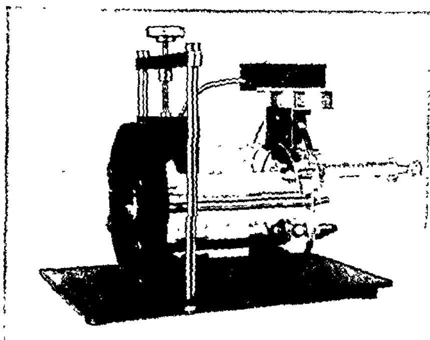


Fig. 111
Perspex hand plethysmograph for use with the R.C.A. transducer valve No 5734

effect will be exaggerated by and during the venous occlusion. Also, changes in the external environment will produce volume changes of the air inside the plethysmograph, although this should be easily avoided by keeping the room temperature reasonably constant. Finally, air is compressible. Water on the other hand is not compressible and so gives rapid transmission of volume changes. Water also has a small coefficent of expansion. Probably the greatest advantage of water filling is that it maintains a more constant limb temperature throughout the study. However, immersion in water is not the normal environment of the human limb. Evaporation from the skin is prevented and an abnormal, even though small, hydrostatic pressure is imposed upon the tissues, in particular the superficial veins. However, we believe that the advantages of water conduction outweigh the possible disadvantages, and in all physiological studies the limb is immersed in water within the *plethymo-*

graph. For the hand and foot the water temperature is best kept at 32°C. and for the forearm and calf 34°C.[2]

In digital plethysmography air conduction is used since most of the objections to its use do not hold for such a small volume system. The main objection of the large coefficient of expansion of air can be almost entirely avoided by having a three-way tap in the conducting circuit so that when records are not being made the interior of the plethysmograph can be opened to the environment. The fact that resting blood flows, whether done in air or water, are so similar suggests that the superiority of water over air conduction is not significant at rest, but when blood flows are maximal the same comparison may not hold.

Position and size of cuffs.—The optimum width for cuffs at the wrist and ankle is about 2″. For forearm flow a 5″ cuff is used and for the calf an 8″ cuff. The cuff should be placed around the proximal part of the limb as close as possible to the entrance into the plethysmograph. If a relatively large distance separates the phethysmograph and the collecting cuff the intervening tissue will swell first when the pressure is applied. On the other hand, when the c[illegible] unde[illegible] whe[illegible] the limb may be sucked out of the chamber. These artefacts can usually be recognised easily and corrected by repositioning the cuff or ignored when the record is being calculated.

Thus for the hand and foot the collecting cuff is wrapped around the wrist or ankle within one inch of the diaphragm of the plethysmograph. But for calf and forearm flows it is difficult to place a cuff distal to the joint and yet between it and the plethysmograph, although in some patients we have obtained good records from the calf using a narrow cuff below the knee. In these cases the collecting cuff is better placed immediately above the joint. A second cuff is applied just distal to the plethysmograph around the ankle or wrist These distal cuffs are inflated to 250 - 300 mm. of Hg when calf and forearm blood flow is being estimated so that no venous return or arterial back flow from the part of the limb distal to and outside of the plethysmograph will introduce an error into the measurement[19] It has to be remembered that this procedure in itself may alter the circulation in the forearm or calf and how much of a change it does produce is hard to determine. In most cases the difference between calf and forearm flows measured with and without distal arterial occlusion though small may be significant.[15, 20]

For digital plethysmography a 2 - 3 mm. wide cuff consisting of a section of Paul's tubing stretched over and taped to a hollow brass ring of a size snugly fitting the digit is used This cuff may be placed immediately proximal to the plethysmograph or at the base of the digit, or thirdly, an ordinary collecting cuff may be wrapped around the wrist (Fig 112). Although immediately proximal to the plethysmograph is ideal, filling is so rapid that

it is difficult or impossible to draw a straight line through corresponding parts of the digital pulses and a large artefact is the rule. The base of the digit is the usual position selected but again when blood flow is rapid calculation is difficult, an artefact is usual, and finally the intervening tissue must fill before the distal phalanx begins to swell. With the collecting cuff at the wrist the latter objection becomes paramount and retrograde swelling of the finger-tip may occur when in fact the actual blood flow is minimal. We have not been able to confirm the observation that flows obtained with the cuff at the wrist are regularly one-third as great as those obtained with the cuff on the finger.[9] In the presence of an extremely rapid blood flow, *e.g.* post-sympathectomy

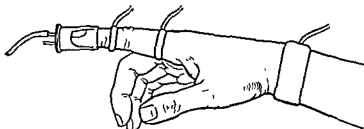


FIG. 112
Plethysmograph on fingertip and cuff showing the three possible positions

flow in hyperhidrosis, the wrist may be the only place a collecting cuff can be placed for measurable readings to be obtained, but generally speaking such instances are uncommon and this position for the cuff undesirable.

Rationale of venous occlusion plethysmography.—The rationale of venous occlusion plethysmography is based upon the assumption that when the collecting cuff is inflated the rate of increase of volume of the part enclosed within the plethysmograph is equal to the rate of arterial blood flow which existed immediately prior to the application of the venous occlusion. In order to make this assumption it is necessary to conclude that the blood flow through bone is insignificant since no degree of venous occlusion is likely to prevent venous return through the bones. In the absence of bone disease, *i.e.* osteitis deformans, the arterial blood flow and venous return through bone is negligible.[8] Also it must be assumed that the venous occlusion pressure commonly used, *e.g* 40 - 80 mm. Hg, is sufficient to occlude all collapsible veins outside of the bones. This seems to be the case. Finally, one must assume that the venous occlusion pressure *per se* does not interfere with the arterial inflow. Although in normal limbs it can be concluded that a pressure of 40 - 80 mm. of Hg does not materially interfere with arterial flow, it is more difficult to disregard such a pressure in limbs the seat of obliterative vascular disease where the blood may be carried predominantly via low-pressure collateral channels pursuing a superficial course around the blocked deep artery In such circumstances the venous occlusion pressure might theoretically obstruct the arterial inflow and so an artificially low blood flow measurement would

result Therefore in venous occlusion plethysmography where one is measuring blood flow through collateral vessels in limbs with obstructed arteries it is best to try a number of collecting pressures and use the highest pressure compatible with unimpaired inflow. By the use of such techniques the resting blood flow in normal limbs and those with obliterative vascular disease are in the same range.[16] Therefore, generally speaking, it may be concluded that venous occlusion plethysmography gives a numerical value for the peripheral blood flow which is close to the actual total amount of blood flowing through that portion of the limb being studied in health and disease.

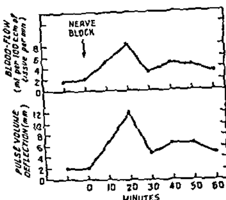


Fig. 113

Digital blood flow and pulse volume before and after ulnar nerve block. (Lancet 17)

Correlation between digital pulse volume and blood flow.—A close correlation between the amplitude of the pulse volume and the actual rate of blood flow in digits has been reported[7, 17] (Fig. 113). Also the pulse volume can be expressed in absolute units. The correlation, however, is not so accurate that it can be substituted for blood flow rate as determined by venous occlusion plethysmography. In physiological investigations where comparisons between the same and other individuals are to be made the venous occlusion method is necessary. Since pulse volume depends

... may give low values when blood flow, in fact, may not be proportionately reduced In clinical practice, however, pulse volume determinations and their response to methods designed to release vasomotor tone in a given individual, will give the clinician most of the information he needs For these reasons we find digital pulse volume of most value in clinical practice and reserve venous occlusion plethysmography for the physiological investigation of the peripheral circulation

Technique and calculation of peripheral blood flow.—In the conduct of a study of the peripheral circulation a number of general principles must be observed The room temperature must be kept constant at 20°C.±1°C. and the entry of people, other than those taking part in the study, must be discouraged The subject must be as comfortable as possible, relaxed and quiet

The part to be studied is placed in the ... been ... arter ... The

effect of the procedure being studied is then tested. This may be indirect heating, the effect of a drug or a peripheral nerve block. From five to ten blood flows are obtained every five minutes or oftener during the period of the study.

When the hand, foot, finger or toe are being studied the collecting pressure is applied for about five seconds at quarter- to half-minute intervals. When the calf and forearm are being studied the arterial pressure cuff is inflated first to exclude the circulation in the limb distal to the plethysmograph.[15, 20] One minute after arresting the distal circulation the venous collecting pressure

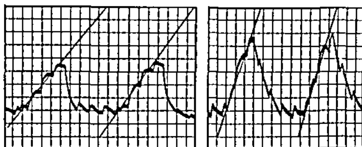


FIG. 114

Blood flow shown by venous occlusion; (*a*) before cervico-dorsal sympathectomy in Raynaud's disease; (*b*) on fifth post-operative day. (*Lancet.*[17])

is applied and the arterial inflow inscribed on the kymograph or photographed. At the end of the study the system is calibrated by injecting a known volume of air; the distance travelled by the recording paper in one minute is marked; and the volume of the part studied is determined by water displacement.

For the calculation of the pulse volume the calibration is compared directly with the vertical height of the subject's pulse wave and the answer converted to c.c. per 5 or 10 c.c. of finger or toe tip. The rate of blood flow is calculated by drawing a line through the tops or bottoms of the first three pulse waves in the curves traced by the increase in size of the part when the collecting pressure was applied (Fig. 114). The rate of blood flow in ml./100 ml. of part/minute is equal to the upward movement of the writing point in centimetres To obtain this the experiment constant, **D**, is obtained from the formula

$$\mathbf{D} = \frac{\mathbf{m}}{\mathbf{XV}}$$

where **X** = calibration reduced to vertical distance the writing point rises with each 1 ml. increment;

V = volume of part in hundreds of millilitres;

m = distance travelled by the recording paper in one minute

A piece of graph paper ruled in centimetres and millimetres is trimmed and the value **D** cm. from the right hand corner is marked. The rate of blood flow

can be read off the recording paper by placing the mark **D** at the point where the sloping line drawn through the collecting curve intersects the base line (Fig 115). The vertical distance from the right hand corner of the paper to its

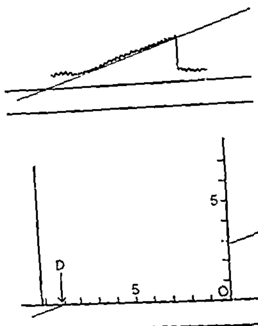


FIG 115

Procedure for calculating the rate of the blood flow from the tracing *Top:* Inflow curve with sloping line drawn and continued through horizontal base line. *Bottom:* Use of graph paper

(Barcroft and Swan—Sympathetic Control of Human Blood Vessels)

intersection with the sloping line is the blood flow in ml /100 ml./minute This method has the advantage that once D is known no further arithmetic is necessary, but a new value for D must be obtained for each experiment and for each part being studied The basis for this method is as follows:

Let X, m and V be defined as above.

D = any given distance in cms. travelled by the paper;

L = upward movement of recording point in cms. while the paper travels D cms;

effect of the procedure being studied is then tested. This may be indirect heating, the effect of a drug or a peripheral nerve block. From five to ten blood flows are obtained every five minutes or oftener during the period of the study.

When the hand, foot, finger or toe are being studied the collecting pressure is applied for about five seconds at quarter- to half-minute intervals. When the calf and forearm are being studied the arterial pressure cuff is inflated first to exclude the circulation in the limb distal to the plethysmograph.[15, 20] One minute after arresting the distal circulation the venous collecting pressure

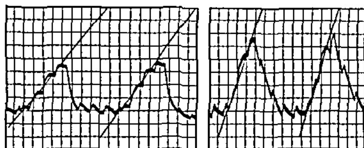


FIG. 114

Blood flow shown by venous occlusion; (a) before cervico-dorsal sympathectomy in Raynaud's disease; (b) on fifth post-operative day. (*Lancet*.[17])

is applied and the arterial inflow inscribed on the kymograph or photographed. At the end of the study the system is calibrated by injecting a known volume of air; the distance travelled by the recording paper in one minute is marked, and the volume of the part studied is determined by water displacement.

For the calculation of the pulse volume the calibration is compared directly with the vertical height of the subject's pulse wave and the answer converted to c.c. per 5 or 10 c.c. of finger or toe tip. The rate of blood flow is calculated by drawing a line through the tops or bottoms of the first three pulse waves in the curves traced by the increase in size of the part when the collecting pressure was applied (*Fig. 114*). The rate of blood flow in ml./100 ml. of part/minute is equal to the upward movement of the writing point in centimetres. To obtain this the experiment constant, D, is obtained from the formula

$$\mathbf{D} = \frac{m}{\mathbf{XV}}$$

where **X** = calibration reduced to vertical distance the writing point rises with each 1 ml. increment;

V = volume of part in hundreds of millilitres;

m = distance travelled by the recording paper in one minute

A piece of graph paper ruled in centimetres and millimetres is trimmed and the value **D** cm. from the right hand corner is marked. The rate of blood flow

CHAPTER VI

THE RADIOLOGY OF PERIPHERAL VASCULAR DISEASE

IN the investigation of peripheral vascular disorders, radiology plays an important and in many ways a decisive part. The method of investigation is not only useful from a purely anatomical diagnostic point of view, but also helps in elucidating some of the many pathological and physiological problems Although most information from the radiological



Fig 116
Calcified atheromatous plaques in the lower femoral and popliteal artery

investigation of peripheral vascular disease will be obtained by contrast studies of the blood vessels, plain radiography of the soft tissues and bones can help in arriving at a diagnosis

F = rate of blood flow in ml./100 ml. of part/minute.

Then

$$F = \frac{Lm}{XDV} \ldots\ldots\ldots\ldots\ldots\ldots 1$$

In any given experiment X, m V are constant. A distance D can therefor be chosen so that

$$D = \frac{m}{XV}$$

Substituting this in equation 1

$$F = \frac{Lm}{XV} \times \frac{XV}{m}$$

$$\text{or } F = L$$

That is, the rate of blood flow in ml./100 ml. of part/minute is equal t the upward movement of the writing point in centimetres.

R. B. L.

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[illegible]

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ARTERIAL CALCIFICATION.—Two main types of arterial calcification can be distinguished.

(1) The atheromatous plaque of the intima, which appears as an irregular, dense shadow in the line of the vessel wall; in the early stages of atherosclerosis this calcification will be localised to a few selected sites such as the middle and lower thirds of the femoral artery in Hunter's Canal, the popliteal artery and the tibial vessels at their bifurcation below the knee joint or just above the ankle joint[1] (Fig 116). Localised atheromatous plaques in the brachial, ulnar and radial arteries are less commonly seen. As the disease progresses scattered calcifications tend to become confluent until in the advanced stages of atherosclerosis the whole artery is calcified and clearly outlined through its entire length. But even when this late stage has been reached, the contour of the vessel appears to be irregular and the calcified shadows are not entirely uniform (Figs. 117 and 118). In atherosclerosis only the major vessels of the limbs are thus *affected* and it is not common to see extensive calcifications in the smaller arteries of the hands and feet



FIG. 119

...situation and size.

(2) The calcification which occurs in Monckeberg's Sclerosis is much more uniform and tubular in appearance than the atheromatous plaques. Calcium is laid down uniform...

A ... type of vascular ... minimal response

THE PLAIN RADIOGRAPH OF THE LIMBS AND ABDOMEN.—*On the soft tissue film of the limbs and abdomen in a healthy patient, arteries will not be visible; superficial veins, however, if surrounded by fat in the sub-cutaneous tissues* may become quite easily distinguishable. They will appear as dense, linear opacities branching into smaller seg- [illegible] present they can become very tortuous. If, on the other hand, the arterial wall is pathological and calcified, that part of the vessel will cast a shadow which will be apparent radiologically.

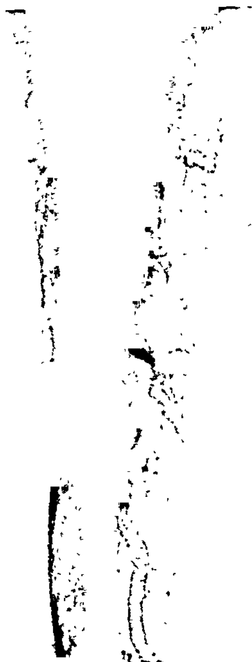


FIG. 117
Extensive calcified atheromatous plaques in the arteries of the thigh.

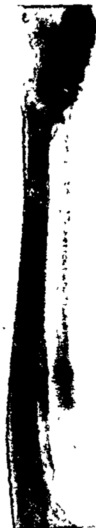


FIG. 118
Extensive calcified atheroma in the forearm.

D, where, in addition to the larger arteries, the smaller ones of the hands and feet are calcified (Fig. 120). These heterotopic deposits are not unlike those ... atherosclerosis. The shadows are irregular and granular and the ... if the whole vessel wall

Calcification of the aorta and iliac vessels. Calcifications in these sites are common in middle-aged and elderly people suffering from atherosclerosis and it is not unusual to see the whole abdominal aorta and iliac vessels clearly outlined in continuity by extensively calcified atheromatous plaques. In the antero-posterior film, the abdominal aorta is seen as a tubular structure superimposed on the spine (Fig. 121). The iliac vessels extend from the fourth lumbar vertebra outwards and downwards into the pelvis, merging finally into the main femoral arteries below the pubic ramus (Fig. 122). The calcified abdominal aorta is best demonstrated on a lateral radiograph of the abdomen and this film also helps to localise calcified shadows associated with the iliac vessels, which are projected well in front of the sacrum (Figs. 123 and 124). Other abdominal vessels occasionally visible, when they are heavily calcified, are the renal arteries, coeliac axis and the splenic arteries (Fig. 125). It is the tubular appearance of the vascular calcifications and their anatomical sites which helps in differentiating them from other calcified shadows such as renal calculi, calcareous abdominal glands, calcified rib cartilage and, rarely, calcifications associated with abdominal tumours. The antero-posterior and lateral films of the abdomen should provide adequate radiographic evidence to establish their nature. Aneurysms of the abdominal aorta and iliac vessels, when calcified, are equally well outlined and demonstrated as such on antero-posterior and lateral films. Not only are soft tissue shadows obvious but



FIG. 121

Extensive calcification of the abdominal aorta and iliac vessels. The calcified abdominal aorta is overlying the spine



Fig 120

Severe calcification in the digital arteries with some calcification in the terminal phalanx of the ring finger Patient with renal osteodystrophy.



FIG 123
Lateral radiographs of the thorax and abdomen. This demonstrates extensive calcified atheroma in the thoracic and abdominal aorta in front of the spine



FIG. 122
Radiograph of the pelvis There is extensive atheromatous calcification in the common iliac, external and internal iliacs The right femoral artery is similarly affected just below the hip joint.



FIG 123
Lateral radiographs of the thorax and abdomen. This demonstrates extensive calcified atheroma in the thoracic and abdominal aorta in front of the spine.

calcifications, either in an extensive thrombus or in the vessel wall itself, often project well beyond the normal anatomical limits of the artery involved At times the actual aneurysmal sac is outlined by such shadows.

Calcification in the veins.—Calcifications (Fig. 126) *in the wall of a vein,* sufficiently extensive to cast a shadow, are exceedingly rare but a calcified thrombus in a vein is often seen, particularly in pelvic phleboliths. These



FIG. 124
See legend under Fig. 123.

appear as solid, round or oval shadows of varying size from a pin head to a millet seed. The commonest sites are in the pelvic veins, but occasionally they can be demonstrated in angiomatous formations and vascular tumours in any part of the body. Learmonth (1951)[2] described some venous calcifications in the portal tree in patients with portal hypertension.

Radiographic appearances of bone in peripheral vascular disease.—Decalcification of the skeleton, particularly of the limb bones, due to disuse atrophy, is a common occurrence in peripheral vascular disorders. The small bones of the feet are more frequently affected than those of the hands. In



FIG. 125
Antero-posterior film of the left upper quadrant of the abdomen There is evidence of a rather tortuous, tubular shadow—atheromatous calcification in the splenic artery

thromboangiitis obliterans, Raynaud's disease, scleroderma and dermatomyositis decalcification of the small bones of the hands and feet is a very frequent feature (Fig 127). If the soft tissues and bones have been subjected to chronic ischaemia due to arterial thrombosis, and there is extensive peripheral vascular occlusion, not only is there likely to be evidence of decalcification, but also marked narrowing and even disappearance of the bony cortex.

Two distinct conditions must be considered. (1) "Bone infection and necrosis." In these there is likely to be evidence of extensive bone erosion with some new bone formation and marked soft tissue swelling (2) "There



FIG. 126
Venous calcification along the lateral aspect of the knee joint.



FIG 127
Thin bones of the hands in a patient with Raynaud's Disease.

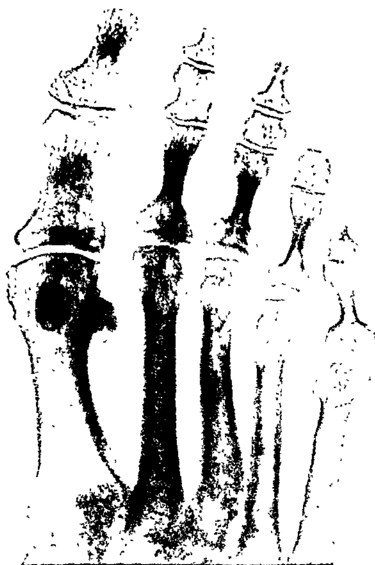


FIG. 128
Forefoot of a patient with thromboangiitis obliterans. The terminal phalanges of the 2nd, 3rd, 4th and 5th toes show early signs of bone absorption and necrosis

is slow disappearance of bone" without evidence of sclerosis or sequestration and distinguished by a gradual destructive process with shortening of the small bones of the hands and feet and eventually complete disappearance (Figs. 128



FIG 129
Foot of a patient with thromboangiitis obliterans The proximal phalanx of the second toe and the fifth metatarsal show very advanced bone absorption and some bone necrosis

and 129) Both phenomena may be present in the same patient. In thromboangiitis and atherosclerosis, infection and bone necrosis are more common, whereas in Raynaud's disease, scleroderma, frost bite, acrocyanosis and



FIG 130

Hand of a patient with scleroderma demonstrating very advanced bone absorption of the phalanges and the heads of the metacarpals with trophic changes at the metacarpo-phalangeal joints There is a similar destructive process in the wrist joint, with considerable bone absorption of the lower end of the ulna

leprosy, bone atrophy and trophic changes involving the joints prevail (Fig. 130) A well-marked periostitis often develops in the underlying bone of

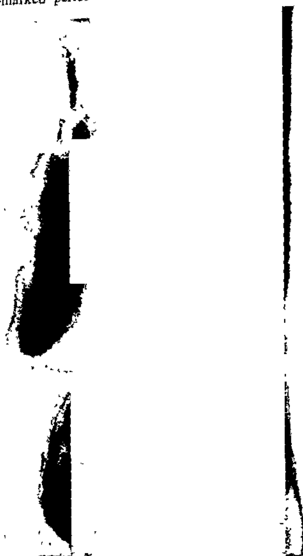


FIG 131
Radiograph of the lower end of the tibia. Patient with a large gravitational ulcer and very marked periosteal reaction of the underlying bones of both tibia and fibula

chronic leg ulcers, but there is seldom severe infection of the bone itself or joint involvement (Fig. 131)

Irregularity of bone growth is a not uncommon phenomenon of arterio-venous fistulae, with overgrowth in length of the affected limb

Bone changes due to vascular soft tissue tumours and aneurysms.—*If* a tumour or aneurysm lies in close proximity to bone, superficial erosions of the cortex, with scalloping of the bone surface are likely to occur. The rate at which bone erosion develops depends upon the rapidity of growth of the tumour and its intrinsic pulsation. Bone erosions of this type due to aneurysms of the abdominal aorta and iliac vessels affect the anterior surfaces of the vertebral bodies and the sacrum. Erosions produced by the popliteal and femoral arteries affect the posterior aspect of the lower femoral shaft. Rarely are bone erosions due to aneurysms seen in other sites of the limbs but vascular tumours, if of some size, can produce similar changes in any other bones of the body. One example is the carotido-cavernous fistula which may erode the sphenoid.

Radiology of the chest.—The incidence of pulmonary thrombo-embolism in peripheral vascular diseases is surprisingly low compared with that of other conditions. If an embolus is large enough to produce a definite pulmonary infarct, a significant pulmonary shadow will be apparent. The radiological signs, however, lag behind the clinical by an interval of a few hours to a day. A number of distinct opacities can be produced: (I) a pulmonary shadow, (2) pleural opacities, and (3) diaphragmatic elevation. Any combination of these three lesions may be present in the same patient. Infarcts may be solitary, but in most cases they are multiple. The lower pulmonary zones are more frequently affected than the upper or middle zones and the right lung is more commonly affected than the left.[3] The most common opacity associated with pulmonary infarction is either an area of localised consolidation due to true haemorrhagic exudation or segmental linear collapse. In Short's[4] series (1951) there was a localised consolidation in 88 per cent In M'Cloud's[3] series (1954) the incidence of this was 62 per cent. Pleural exudates are also common; Short records an incidence of 56 per cent. and M'Cloud one of 46 per cent. Diaphragmatic elevation in Short's series occurred in 39 per cent. but in our experience the incidence of diaphragmatic elevation is not so high.

It is rare to see the classical radiographic sign in pulmonary infarction, *i.e.* the triangular or oval opacity of homogenous consistence with its base at the periphery of the lung and its apex pointing towards the hilum (Figs. 132 and 133). If the infarct extends towards the periphery of the lung, pleural effusions are common; they may be encysted if the inter-lobar fissure is involved

Pulmonary shadows, since they are not necessarily specific of infarction. must be differentiated from shadows caused by pneumonia, encysted effusions or even peripheral neoplasms. If the infarcted area is not too large, resolution of the shadows is rapid—within days—but occasionally resolution can be delayed for longer periods even of weeks and, finally, residual opacities may be retained as a result of extensive scarring at the site of the original infarction The time relationship between the clinical phenomena and the radiographic

appearances, and their progress, which can vary from day to day, is of considerable importance in the diagnosis Chest radiographs on the ward, or preferably in the X-ray department, should be taken as soon as possible. They



FIG. 132
Antero-posterior radiograph of the chest This demonstrates an extensive area of consolidation in the right cardio-phrenic angle due to a massive infarct The right lower lobe pulmonary artery leading towards the infarcted segment is considerably dilated

should then be repeated at intervals to cover the clinical course of the disease, and only then will it be possible in most instances to arrive at a satisfactory diagnosis by a correlation of the clinical findings with the radiographic appearances.

Another feature which must be considered in the chest is occasional cardiac enlargement as a manifestation of a large arteriovenous fistula. In

scleroderma there is often evidence of extensive pulmonary fibrosis which is progressive and which may involve the whole lung. This sclerodermatous effect of progressive fibrosis can also be found in the alimentary tract, in the stomach, oesophagus or small bowel, for example.

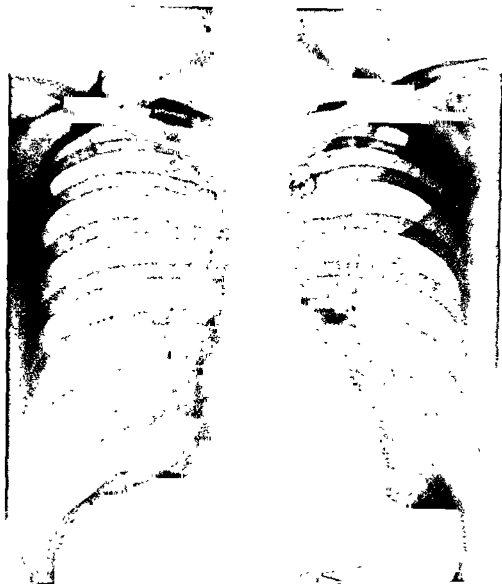


FIG. 133
Postero-anterior radiograph of the chest. This demonstrates a small, oval opacity at the left base towards the peripheral lung field, due to a small pulmonary infarct

In barium studies, organs affected by the progressive fibrosis of scleroderma appear rigid and the normal mucosal pattern is obliterated. The passage of the barium through the alimentary tract is accelerated.

PERIPHERAL ARTERIOGRAPHY

HISTORICAL NOTE.—The first successful attempt to demonstrate the peripheral vessels by X-rays was made in 1896 by Haschek and Lindenthal,[7] who

injected radio-opaque material into an amputated leg Since then this method of demonstrating blood vessels in anatomical specimens has become routine practice in departments of anatomy. The types of contrast media used vary, but any material which is opaque to X-rays and flows freely when injected, such as barium in gelatine, red lead, etc., give adequate and satisfactory radiographs. In 1923, Berberich and Hirsch[6] were the first to carry out a successful arteriogram on a living subject. From then on many reports of the application of this method have appeared in the literature and since 1931, when organic iodides were introduced for the injection of peripheral vessels, arteriography has established itself as useful procedure in the investigation of peripheral vascular disease. The earlier work on peripheral arteriography was extensively reviewed by Edwards in 1933[7] Publications in the last few years have been innumerable and many excellent papers have appeared in the literature. Lindbom in 1950[r] brought the review up to date and discussed not only pathological findings, but also modern methods and technical developments.

A. *Indications for peripheral arteriography.*—In the investigation of peripheral vascular disorders, the clinical information gained from a careful examination of the patient will, in most cases, provide adequate data for the management of his complaints. If, however, additional information is required about the state of the vessels, arteriography, as was shown by Messent *et al* in 1953[8] is the best ancillary method of investigation. Arteriography accurately demonstrates the presence of organic disease and shows the level and extent of an arterial block It gives information about the state of the vessels distal to the block as well as demonstrating the extent of the collateral circulation

Indications for peripheral arteriography include:—

1 Obliterative arterial disease, to confirm its early presence; to localise the site and extent of thrombosis for such surgical treatment as arterial grafting and end-arterectomy; and to demonstrate the degree of development of the collateral vessels around to the thrombosed artery ; this last point is a guide in the selection of amputation levels.

2 In aneurysms—to establish the diagnosis, to demonstrate accurately the site and extent of the lesion, and to help in the planning for possible surgical resection.

3. To outline, if possible, an arterio-venous fistula, and

4. In vascular tumours, of soft tissue or bone, as an aid in differential diagnosis

B. Contrast media.—A great variety of substances have been used for arteriography, but not until the organic iodides were developed for urography was a safe medium available 35 - 50 per cent. Diodone is the contrast medium of choice for peripheral arteriography.

Learmonth in 1944[9] reported on the use of this substance without ill effect in a large number of examinations. We have used it for many years and have always found it a most satisfactory medium. If injected into the soft tissues, apart from slight local discomfort, there will be no ill effects. Diodone is rapidly absorbed and excreted in the urine. Before the arteriogram is done, it is advisable to test the patient for iodine sensitivity. This is best achieved by intravenous injections of 1 c.c. which should be tolerated quite readily. If, however, there is any reaction, such as slight increase in the pulse rate, coughing or discomfort, or the appearance of a rash, then the patient is sensitive. In this case a desensitisation course must be given and when completed, the contrast medium can be injected with safety. Daily intravenous injections of small quantities of Diodone are given, starting with 0·5 c.c., and increasing the amount over a week to about 10 c.c.[10]

Seventy per cent. Diodone should in no circumstances be used, for peripheral arteriography. Its introduction into an artery of small calibre is dangerous. Lindbom[1] (1950) quotes two cases of supervening gangrene of the lower limb after its injection and subsequent thrombosis of the femoral artery. He advocates 35 per cent. solution for peripheral arteriography rather than 50 per cent. solution. In our experience 35 per cent. gives a less satisfactory shadow than 50 per cent. We have only had one accident which could not be ascribed to the concentration of the solution. The other important contrast medium which is being used in the country is Thorotrast, a radio-active substance. Intra-arterial injections of this substance are painless. Thorotrast, however, is not excreted by the kidneys but is fixed in the reticulo-endothelial system. Because of its radio-active properties, it may have dangerous after-effects, such as the development of malignant disease.[11] Allen and Camp[12] (1937) and Yates and Coe[13] (1937) however, claimed it to be harmless in small quantities and they have used it repeatedly for peripheral arteriography In Germany before the war, Degkwitz[14] in 1938 reported on Iodosol (ethyl-tri-iodostereate) which he claimed to be a very useful contrast medium not producing any untoward reaction and which was tolerated very well by patients.

Twenty c.c. of Diodone is an adequate amount to outline the arteries in the lower limbs from groin to toe and 10 to 15 c.c. are necessary for the upper limb. Injection of Diodone into the artery will produce vaso-dilatation with hyperaemia within seconds if the arterial tree is normal. If major blocks are present, pallor of the skin where the blood supply is inadequate sometimes persists throughout the whole examination. Repeated injections are tolerated well, provided at least twenty minutes elapses between them, and we have injected up to 60 c.c on a number of occasions into the femoral and brachial arteries without untoward effect.

Technique of Arteriography.

GENERAL CONSIDERATIONS.—Percutaneous injection of contrast medium is the method of choice in peripheral arteriography, since exposure of an artery

turns a relatively simple procedure into a formal operation. If percutaneous injection fails, or the artery cannot be defined accurately by palpation, surgical exposure of the artery and injection under direct vision may be necessary. This is a safer procedure than repeated attempts at percutaneous arterial puncture.

Arteriography should be carried out under general anaesthesia, since this avoids pain produced by arterial puncture and the intra-arterial injection of contrast medium; it also prevents movement of the limb which would spoil the radiograph, and induces maximum vaso-dilatation. Lindbom[1] (1950) prefers local anaesthesia; Learmonth[15] (1940) suggests a spinal anaesthetic. Under local anaesthesia the method may be satisfactory in the majority of cases, but in some it will be inadequate, particularly if contrast media of 50 per cent. solutions are used, when pain and discomfort will be so marked that movement of the limb will be unavoidable. 35 per cent. Diodone is less painful when injected intra-arterially, but with this concentration, adequate visualisation of the arteries, particularly of the peripheral branches, *i.e.* hands and feet, is not always achieved.

Injection technique of the femoral artery.—Arteriography of the lower limb should only be carried out if there is a palpable pulse in the femoral artery below the inguinal ligament. If the pulse is absent, aortography is necessary as an arterial block is most likely either in the aorta or iliac vessels.

Through a No. 18 short bevel needle, 20 c.c. of Diodone are injected into the femoral artery *just below the* inguinal ligament. The stream of contrast medium should be in the *direction* of the blood flow and the needle inserted accurately and well *within the lumen of the* artery to avoid extravasation of the contrast medium, or intra-mural injection, which will produce considerable pain and discomfort *when the* patient is again conscious. The flow of blood back into [illegible] position of the nee[illegible] possible, while the [illegible] the operator himself [illegible] the contrast mediur[illegible] adequate filling of the smaller foot vessels. Dos Santos[16] (1935) and Lindbom[1] (1950) suggest mechanical injection by compressed air, to move the syringe piston. This ensures a constant speed and more rapid injection. It is, however, unnecessary to go to all this trouble as manual injection with an adequate *syringe will* give satisfactory results.

Lindbom[1] (1950) *suggests*, as an alternative, *injection of the* contrast medium *against the blood* stream. By this *method* it will be possible to outline in every case the superficial femoral and deep *femoral* arteries should the puncture *site* be distal to the bifurcation of the [illegible]

[illegible] necessary. We find that to achieve [illegible] of the profunda with contrast medium *it is* essential to puncture the

femoral artery just below the inguinal ligament, as even a very high division of the profunda and superficial femoral will rarely extend to this point. If the artery is transfixed, as often happens, on slow withdrawal of the needle, blood will rush back into the syringe when the lumen is re-entered. This will be of no consequence and even multiple punctures, although not desirable, are tolerated well.

Radiographic technique for arteriography of the lower limb.—A cassette tunnel, of a size adequate to cover the whole length of the limb from groin to toe, is essential. It should be wide enough to hold 15″ x 12″ X-ray cassettes[17] We have used a simple cassette tunnel made of plywood, which in one instance was of a size to cover both limbs, and in another instance was long and wide enough for one whole leg. This latter type of cassette tunnel is perfectly adequate for most angiographic procedures. More elaborate apparatus has been developed in Scandinavia and Germany. In one instance the cassettes are so arranged in the tunnel that by a simple withdrawal of leaded diaphragms, individual cassettes which were protected against radiation, can be exposed without removal of the cassettes, and after this is done, the leaded diaphragm is replaced to re-protect the exposed films against further X-radiation. Alternatively, one cassette can be used, which is large enough to cover the entire limb and a number of these can then be placed in position and withdrawn mechanically at rapid intervals. Or a strip film can be used which is moved mechanically and is fixed between two intensifying screens for each individual exposure.[18]

The lower limb is placed on the cassette tunnel with the foot externally rotated. This can be done either by bending the limb at the knee, or by an assistant who holds the foot in the appropriate position By external rotation of the limb, the arteries are, to some extent, projected away from the overlying bone structure in the antero-posterior position.

When using standard radiographic films it is possible to cover the entire limb with three 15″ x 12″ cassettes which gives adequate room for overlap of the individual radiographs. Alternatively one large cassette can be used which extends from groin to toe.

When individual cassettes are used, rapid changing of these is essential and this is then followed up by repeated radiographic exposure. Cassette changing can be done either manually or mechanically and the speed of this will depend partly on the suspected pathological condition. If the blood flow is normal or an arterio-venous fistula is suspected, very rapid changing is essential. If, on the other hand, some delay in blood flow is suspected as indicated by an absent pulse in the major arteries, changing must be slightly delayed. Under normal conditions, the whole radiographic procedure should not take longer than fifteen to twenty seconds.

In addition to the routine described above, further views of the foot can be taken if an accurate study of the circulation in this area is required. By moving the X-ray tube along its tube stand along the limb after each individual

exposure and re-centering it over the cassette which has been placed into the cassette tunnel under the limb, very adequate and satisfactory arteriograms of the entire limb can be obtained.

With our radiographic technique, the film/tube distance is 36″. Alternatively one can work at a longer film/tube distance of 72″ and with a specially-shaped cone the whole limb can be radiographed in one exposure. Or a slit

radiographic team should give satisfactory results. It is not necessary to use complicated and highly-specialised equipment as simple devices are quite satisfactory in every respect. The lateral projection is not essential as the antero-posterior view will be adequate for most purposes. The radiographic factors depend on the X-ray apparatus used, but basically a kilovoltage of 80 for the thigh and 65 for the foot at a distance of 36″ and a time variation of $\frac{1}{8}$ to $\frac{3}{8}$ seconds will produce satisfactory results.

Upper limb.

GENERAL CONSIDERATIONS.—For the upper limb the same general points which were discussed previously for the lower limb hold good, but the volume of 50 per cent. Diodone injected is diminished to 10 to 15 c.c. This amount will be adequate to produce satisfactory filling of the brachial and digital vessels

Injection technique.—Radiographic demonstration of the axillary and brachial vessels is exceedingly difficult without formal exposure of the vessel. However, direct puncture of the third part of the subclavian and axillary arteries is possible in some instances The arteries of the forearm can best be demonstrated by direct puncture of the brachial artery in its middle third or at its bifurcation just above the elbow joint.

A short bevel 19 gauge needle is used, which must be well inserted into the arterial lumen as in the case of the femoral artery. Blood flow through the limb, if the injection is carried out into the

is injec

diastol pulse beats, and at once raised to a level above the systolic arterial pressure. After this the second film is exposed.

The injection of 50 per cent Diodone into the

in which the arterial flow has been obliterat

of the skin which is proof of true intra

injection

Once the arterial flow is re-established, the blanching disappears and an immediate reactive hyperaemia will be noted.

femoral artery just below the inguinal ligament, as even a very high division of the profunda and superficial femoral will rarely extend to this point. If the artery is transfixed, as often happens, on slow withdrawal of the needle, blood will rush back into the syringe when the lumen is re-entered. This will be of no consequence and even multiple punctures, although not desirable, are tolerated well.

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In addition to the routine described above, further views of the foot can be taken if an accurate study of the circulation in this area is required By moving the X-ray tube along its tube stand along the limb after each individual

THE INTERPRETATION OF THE NORMAL ARTERIOGRAM

General observations. — Streamlining of the contrast medium, just distal to the site of the injection further along in the arterial tree, is not an



FIG. 134
Arteriogram of the thigh. The profunda femoris is clearly outlined. Note the rather tapering edge and less dense superficial femoral artery. The appearances are produced by streamlining

infrequent occurrence, particularly if the radiograph is prematurely exposed and the contrast medium is just beginning to outline the vascular lumen. These

Radiographic technique.—As in the lower limb procedure, the patient's arm is placed on a cassette tunnel which extends from the axilla to beyond the finger tips; in fact the same tunnel can be used for both upper and lower limbs. The hand is spread out in supination and held in this position by cellotape strips. Multiple X-ray exposures are necessary—from five to six—to cover the arterial and venous circulation. The speed at which these exposures are made depends on the speed at which the arterial flow in the arm is controlled by the sphygmomanometer. On an average exposures should be made at three to four seconds intervals. Excessive speed is unnecessary and may outstrip the actual blood flow and contrast delineation of the vessels. 12" x 10" cassettes are satisfactory for the hand and wrist, but if the forearm is included, 15" x 12" cassettes are necessary. Where the whole arm is to be examined, two 15" x 12" and a 12" x 10" cassette, or one long cassette covering the limb from axilla to the finger tips can be used. When the subclavian and axillary arteries are to be investigated, the patient's shoulder should be placed well on to the cassette tunnel with the arm outstretched and a preliminary film should be taken to avoid unsatisfactory centering. As in the lower limb, standard radiographic equipment is adequate for the radiographic procedure, although more elaborate and complex mechanical apparatus can be used for the upper as for the lower limb. For the hand and forearm, tube movement and re-centering is unnecessary when individual exposures are made, but if the whole limb is to be investigated, the tube can either be moved or the long distance technique, as for the lower limb, can be employed.

Complications of peripheral arteriography.—The most serious complication is the precipitation of arterial thrombosis, either at the injection site or distal to it, induced by the arterial puncture or by the injection of contrast medium. This complication is the main reason why arteriography should not be carried out lightly as a routine method in the investigation of every case of peripheral vascular disease.[20] In a series of more than 300 peripheral arteriograms done at Hammersmith Hospital, one patient developed thrombosis at the site of arterial puncture two weeks later, following an operation for lumbar sympathectomy, and amputation of the limb was required. The operation was prolonged and accompanied by a period of shock as a result of severe haemorrhage. Haematoma formation at the site of the puncture, or peri-arterial injection are less serious complications and do not cause permanent damage. The application of local heat and the injection of a normal saline with hyalase into the soft tissues will speed up re-absorption of the contrast medium and decrease the local reaction.

The dislodgement of atheromatous plaques at the injection site and the development of arterio-venous fistulae have been reported by some observers,[21] but we have no experience of either of these complications.

medium and it is only in the region of the major joints that they are demonstrated. These smaller vessels nearly always take a straight and well-defined anatomical course. They are of relatively small calibre in relationship to the major vessels from which they arise.

Arterial spasm.—There is distinct narrowing of the arterial lumen which retains its smooth contour at the site of injection. This is not an unusual appearance and can be visible in quite normal arteriograms when the narrowed section can extend over a few centimetres. If, however, serial films are taken, the spasm will be seen to disappear within seconds and the arterial lumen will return to its normal size (Figs 135 and 136). Thus, variations in calibre of the artery on serial radiographs always indicate spasm and do not imply organic disease If, however, the narrowed segment persists, is of irregular contour and is a constant feature on serial radiographs, it can only be due to an organic pathological process

The appearances of the normal arteriogram in the lower limb.—Distal to the point of injection, below Poupart's ligament, all major arteries can be outlined satisfactorily. The vessel walls are smooth and their calibre diminishes gradually towards the periphery. In the thigh only the superficial femoral and profunda femoris are clearly outlined—the muscle and skin branches rarely fill. Around the knee, the descending geniculate and other geniculate vessels can clearly be distinguished and so can the poplite[illegible]
tibial and posterior tibial as well as the peronea [illegible]
and so are a small number of muscle branches ([illegible]
anatomical variations are not infrequent, such as absence of the dorsalis pedis and minor variations involving the plantar arch and [illegible]

[illegible] much more numerous than the arteries. They are wider, their anatomical distribution is less constant and they are of smooth contour and run a straight course (Fig. 139). Only a qualitative assessment of the circulation can be made on the appearances of the vascular pattern. A quantitative assessment, even with accurate estimation of the circulation time, is unsatisfactory.

The appearances of the normal arteriogram in the upper limb.—As in the lower limb, all major arteries distal to the point of injection are demonstrated, such as the brachial, ulnar and radial arteries, the interosseous branch and the palmar arch as well as the digital vessels and the smaller vessel in the pulp of the finger Venous filling is often seen in the later films of the arteriographic series. Muscle and skin vessels are not outlined except for a few branches in the region of the elbow joint and above the wrist

To obtain an adequate arteriogram of the smaller palmar and digital vessels, the contrast medium must be injected into the brachial artery at the

appearances can be mistaken for arterial thrombosis but the rather indefinite, tapering edge of the streamlining and the absence of collateral vessels in the





FIG. 135 FIG 136

FIG 135 Arteriogram of the popliteal artery, lateral projection There is a *smooth narrowing of the popliteal artery.*

FIG. 136 Same case as Figure 135. The narrowing has disappeared and the *artery is of normal calibre These appearances are due to arterial spasm* These films were taken within two seconds

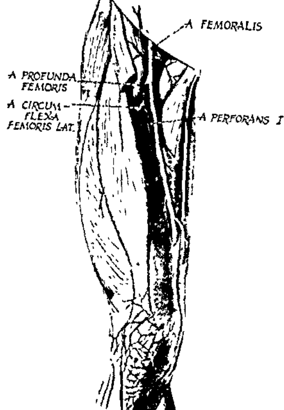
vicinity will differentiate the appearances from a true arterial block[17] (Fig. 134) *Smaller vessels supplying the skin and muscles do not always fill* with contrast

elbow joint (Fig. 140). If the injection is made distal to this point as, for example, into the radial artery, filling of the digital vessels of the little and ring fingers is often inadequate. The appearances of the vessels, *i.e.* their contour and calibre is very similar to those in the lower limb.



FIG 139
Normal arteriogram of the lower limb This shows simultaneous filling of the arteries and veins in the lower calf and foot The calibre of the veins is larger than that of the arteries and they are very numerous

The arteriographic appearances of the collateral vessels.—When muscle and skin branches which normally do not fill take over the collateral circulation they can easily be distinguished by their tortuosity and their anatomical



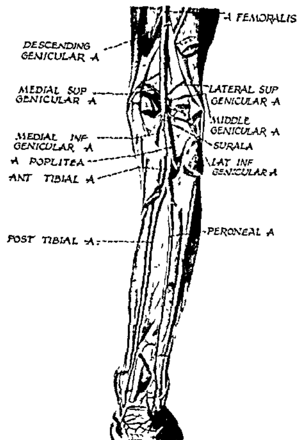


FIG. 137

PROFUNDA FEMORIS
FEMORAL ARTERY
MEDIAL SURAL ARTERY
POPLITEAL ARTERY
ANTERIOR TIBIAL
PERONEAL
POSTERIOR TIBIAL

FIG. 138

FIG. 137. Diagrammatic representation of the arterial system of the lower limb.

FIG. 138 Normal arteriogram of the lower limb

FIG 141

Arteriogram of the thigh Thrombosis of the temoral artery in Hunter's Canal with a satisfactory colla-
just
re er



FIG 142

Arteriogram of the thigh The profunda fer-
ficial femoral arteries are clearly outlined Th
superficial femoral artery is slightly irregu
early atheroma There is no evidence as
filling which is usually absent at this early sta
process.

position. They are frequently as wide as major arteries, from which they arise Their sites of origin and re-entry into major vessels are often bizarre and may occur at right-angles. If they carry the circulation around an arterial block,



FIG. 140
Normal arteriogram of the hand This shows very satisfactory filling of the radial and ulnar arteries at the wrist, palmar arch and digital vessels There is also early venous filling

they arise just proximal to the arterial thrombosis and may re-enter the major vessel distal to the blocked segment (Fig 141). Their numbers and variations depend (1) on the extent of the arterial block, and (2) on the size of the vessel involved. If major muscle branches are available to carry the collateral

The arteriographic appearances of atherosclerosis.—In this interpretation the following points must be considered—(1) persistent changes in the contour of a vessel wall, such as narrowing or widening of the lumen, or irregularity in contour; (2) arterial blocks—their extent and number; (3) the presence of collateral vessels—their site, calibre and number; (4) the delay of re-filling of vessels distal to major arterial blocks; (5) the presence of venous filling on later serial films and its extent

The arteriographic appearances in the lower limb.—The earliest sign of degenerative arterial disease is a slight persistent irregularity of the vessel wall or persistent change in the calibre of a major artery (Fig 142). This irregularity often coincides with calcified atheromatous plaques which may be visible on plain films. On the arteriogram they fit very closely into filling defects (Figs 143 and 144). In the later stages of the disease these irregularities and contour changes become more numerous and extensive. Their commonest sites are the middle and lower thirds of the femoral artery, the popliteal artery and the tibials just distal to their origin. In the advanced stages of the disease, the irregular filling defects and constrictions of the vascular lumen become generalised until all major vessels in the thigh and calf appear to be affected. At any stage of the disease process arterial blocks may appear. The commonest site is the lower third of the femoral artery, at the level of the adductor hiatus (Fig. 145). The arterial block is very short at first but this can spread proximally and distally until the whole femoral and popliteal artery is involved (Fig 146) The end points of the block are usually determined by major collateral vessels and the thrombosis tends to spread proximally or distally to where these arise or re-enter.



FIG. 145
Arteriogram of the femoral artery. This demonstrates a very short block and filling of collateral vessels just above the block

In the lower third of the femoral and in the popliteal artery, the levels are usually determined by geniculate vessels. If the thrombosis spreads beyond these collaterals, an extensive section of the artery can be obliterated. If this

circulation or if the collateral circulation is established in the vicinity of a joint, they can indeed be very numerous and large. If the supply of these muscle branches and collaterals around a joint is inadequate, even small

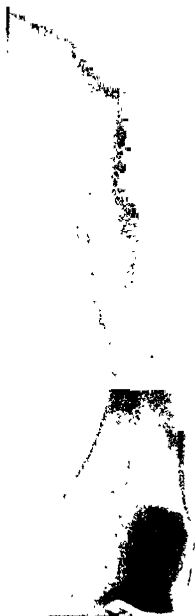




FIG. 143 FIG 144

FIG. 143 Plain film of the thigh shows extensive calcified atheroma in the lower femoral and popliteal arteries

FIG. 144 Arteriogram of the same area shows the calcified plaques which fit very closely into the irregular filling defects in the arterial contour.

arteries of the skin can develop into extensive collateral channels Collateral vessels are easily recognised, not only because muscle and skin branches which normally do not fill are outlined by contrast medium, but also because they are often tortuous from elongation.

normal. If, on the other hand, the collateral circulation is inadequate, re-filling of the main artery distal to the block can be unsatisfactory and this often indicates an extensive thrombosis. The smaller vessels in the lower limb and the vessels in the foot will then not be demonstrated.



Fig. 150
Arteriogram of the lower limb just above the ankle joint which demonstrates a patent anterior tibial and peroneal artery. The posterior tibial is thrombosed The circulation to the foot, which is very good, is carried largely through the peroneal which anastomoses with the posterior tibial just above the ankle joint (Same case as Fig. 148)

An accurate quantitative assessment of the collateral circulation on radiographic evidence alone cannot be attempted. The most valuable guide is re-filling of the major vessels distal to the blocked section, the speed of its occurrence and the adequacy of the circulation beyond this point Venous filling on the later films of the series is also a good sign of a satisfactory circulation This venous filling may occur in the presence of a major arterial thrombosis particularly in the thigh, but is rarely seen if the block is in the popliteal or tibial arteries or if the thromboses are multiple. If venous filling is absent on later films of the arteriographic series, and the examination is technically adequate, it is indicative of a significant decrease in the circulation A less reliable guide is the assessment of the vascular filling of the smaller vessels of the foot. Non-filling of these arteries and a significant diminution in their calibre can only be accepted as a reliable guide of impaired circulation if the affected vessels show definite blocks Minor thromboses in the plantar arch or in the smaller vessels of the foot are frequently seen and



at *right* angles to the main vessel and there can be considerable narrowing of the arterial lumen with a significant degree of irregularity. The collateral vessel appears to be nipped at first in the arterial wall and is then *slightly dilated* distal to the narrowed segment. The calibre of these major collaterals can be nearly as wide as that of a main artery and they often re-enter the main artery distal to the block. The appearances at the site of re-entry are in many ways identical to those at the site of origin (Fig. 151).

In major thromboses of the superficial femoral artery, the collateral circulation to the leg is often established through the *profunda femoris and popliteal arteries.*

In major thromboses of the popliteal, the collateral circulation is carried through the geniculate vessels with additional smaller muscular arteries extending from the femoral to the tibials.

In the presence of tibial thrombosis, of either the anterior or posterior branches, the peroneal carries the bulk of the blood, together with collaterals in the calf which tend to re-enter the posterior tibials just above or below the malleolus, or communicate with the anterior tibial above the ankle joint (Figs. 152 and 153)

The adequacy of the circulation depends on the number and size of the collateral vessels and the degree of re-filling of the major artery distal to the block If this is good, a very adequate arteriogram of the vessels distal to the block can be obtained and the smaller arteries appear relatively

FIG. 149

Arteriogram of the lower limb in the region of the *knee joint* This shows popliteal thrombosis with a very good collateral circulation around the knee joint. *Good filling* of the tibial arteries just distal to their *bifurcation*



FIG 153

Further views of the lower limb, shows good filling of the peroneal artery which carries the entire circulation to the foot and communicates with the posterior tibial artery behind the malleolus The filling of the smaller vessels in the forefoot is not very adequate This is same case as Figure 152.

then the smaller branches arising from the thrombosed segment will also fail to fill. This will then indicate localised ischaemia (Fig. 154).

The arteriographic appearances in the upper limb.—The interpretation of the appearances of degenerative arterial disease in the upper limb are similar to these in the lower limb. Arteriography is infrequently done in the arm, and so the appearances are not so well established.



FIG. 151



FIG 152

FIG. 151 Localised view of the superficial femoral artery just below the area of thrombosis It shows the re-entry of the major collateral vessel at a right angle and how this collateral vessel is narrowed just at the point wh[illegible] femoral artery The femoral artery at this

FI[illegible] int

The arteriographic appearances in medial disease. — **"Mönckeberg's sclerosis."**—In this condition the arteriogram of the limb will demonstrate arteries of normal calibre and no significant contour changes, except for a little serration of the arterial wall produced by the medial sclerosis. Collateral

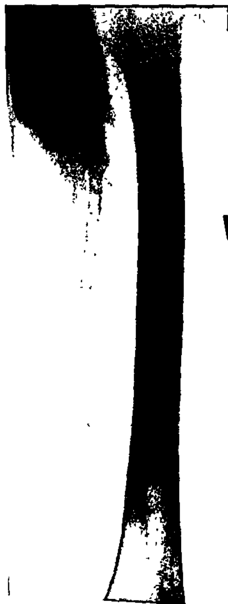


FIG. 155

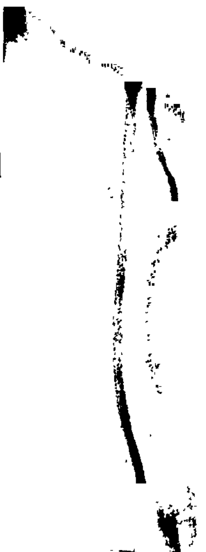


FIG. 156

FIG. 155 Plain film of the thigh. Patient [illegible]
calcificati[illegible]

FIG. 156 Arteriogram of [illegible]
of the profunda femoris ar[illegible]

vessels are not filled and demonstration of the peripheral arteries in the foot and the speed at which they are filled is within normal limits. Early venous filling on serial radiographs is common. In comparing the plain film of the



FIG. 154
Arteriogram of the foot Shows a patent anterior and posterior tibial artery of good calibre There is a short section in the plantar arch of inadequate filling, due to localised thrombosis in the plantar arch

limb and the arteriographic appearances, one can superimpose the calcified vessel very easily upon that outlined by the contrast medium and see how closely the calcifications coincide with minor contour defects in the vessel wall[1] (Figs. 155 and 156). The appearances and the interpretation of the upper and lower limb arteriograms are identical.

Buerger's disease.—In this condition, it is more common for the small peripheral vessels of the limbs to be first affected and it is not unusual, therefore, to obtain relatively normal arteriograms of the major arteries. Once the disease is well established and has spread proximally, extensive thromboses are demonstrated affecting distal segments of major arteries, such as the tibials and

peroneals in the lower limb or the radial and ulnar arteries in the upper limb, as well as thromboses of the smaller arteries in the hands and feet (Figs. 157 and 158). With further progress of the disease process, the arterial blocks spread proximally to the popliteal and femoral vessels in the lower limb and to the brachial in the upper limb. The limits of the thrombosis are nearly always clear cut and regular, the lower limit corresponding, as in degenerative arterial disease, with a point where collateral vessels re-enter. These are very often numerous, tortuous and small, represented by a large number of muscle and skin arteries. Rarely is the main vessel patent distal to the thrombosis if the disease process has affected primarily the peripheral vessels. When, however, major arteries are first involved, such as the lower end of the femoral or the popliteal artery, collaterals which can be outlined by arteriography are seen to re-enter the main vessel distal to the block, and the appearances can be indistinguishable from degenerati[illegible] ... find very ... up to the ... case the circulation to the limb is carried entirely through the profunda femoris from where the collaterals arise.

The arteries proximal to the sites of the thromboses in Buergers' disease are smooth and in no way deformed or tortuous, and they show no significant atheroma. Their lumen, however, may be narrowed and this narrowing which again is quite smooth and uniform, may be localised to a segment of the major vessel. If this narrowing is extensive, collaterals will appear to by-pass the affected arterial segment, this being particularly noticeable in the region of the popliteal artery. In less well established cases, where the disease is quite peripheral, the thrombosed arteries are confined to the foot and hand and the circulation is maintained by fine muscle and skin vessels. In a well established case, where significant thromboses have occurred, venous filling on later serial radiographs is most unusual and there is always gross impairment of the circulation to the affected parts.

The [illegible] ... the arterio-graph ... [illegible]ion is usually much [illegible] extensive. Rarely will the obliterative process spread beyond the radial and ulnar vessels. The arteriographic differentiation of Buerger's disease from degenerative arterial [illegible] ... Atheroma, even of a v[illegible] ... The distribution of ... tends to be distal in Buerger's disease and more proximal in degenerative arterial disease; exceptions do, however, occur as discussed previously. Collateral vessels in Buerger's [illegible] small [illegible] ...

[illegible] arteries are obstructed; in ... arterial disease the main vessels are often patent distal to the block. In some cases, however, the differential diagnosis will be impossible, particularly in the proximal type of Buerger's

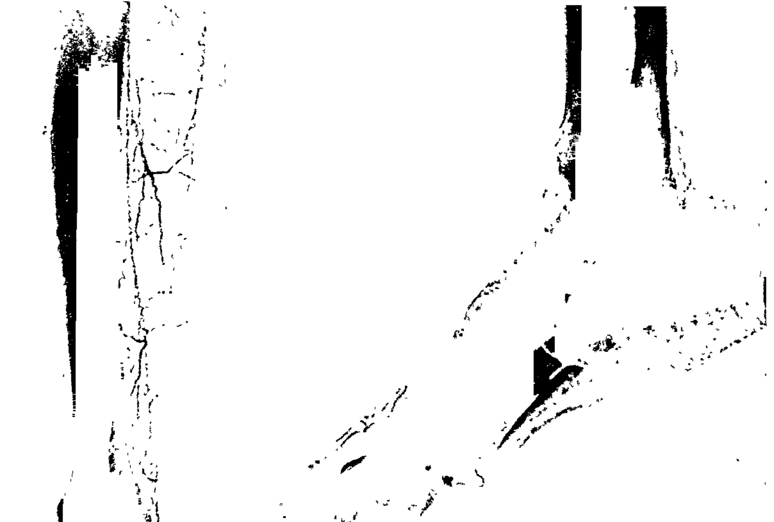


Fig 157

Fig 158

Same patient as Figure 157. Arteriogram of the foot which demonstrates the very inadequate circulation through small, tortuous collateral vessels.

Fig. 157 Arteriogram of the lower limb below the knee joint. Patient with Buerger's Disease *Innumerable small collateral vessels filled as well as a short* section of the posterior tibial artery which partly re-filled through these collaterals Note the small calibre of the collateral vessels and their very tortuous course

disease when there is isolated obstruction of the lower femoral and popliteal arteries, or where the patient with Buerger's disease has superimposed degenerative arterial disease.

THE ARTERIOGRAPHIC DEMONSTRATION OF ARTERIO-VENOUS FISTULAE

The demonstration of vascular fistulae depends entirely upon their position. The more proximal the lesion and the larger the vessels involved, the more difficult it is to demonstrate the communication because of the very extensive shunt from artery to vein. If the fistulae are localised and not very diffuse, their demonstration is possible, but if they are widespread and multiple, arteriography will fail. Congenital arterio-venous fistulae can rarely be demonstrated by arteriographic means.

The technique of investigation.—If the site of the fistula can be clinically localised, serial films of the area must be taken rapidly, starting a second or two after the beginning of the injection. If a mechanically operated X-ray cassette changer is available, this can be used with advantage. Alternatively, manual cassette changing with the aid of a tunnel can give equally good results, and it may help if the arterial flow is partly obliterated proximal to the injection site so that the speed at which the arterio-venous shunt takes place is diminished.

If the exact site of the fistula is not localised, the whole limb should be investigated using the same technique as that used for peripheral arteriography in degenerative arterial disease. It is however essential to obtain rapid film changing and to diminish the arterial flow to the limb, either by digital pressure on the artery just proximal to the [illegible]
cuff.
fistula [illegible] ...lt by the appearance of
[illegible] case a second injection
[illegible] carried out at the sus-
[illegible]

The technique of injection, and the types and quantities of contrast medium used are identical with those in peripheral arteriography in degenerative arterial disease, but the whole process is more rapid.

The appearances and interpretation [illegible]
nomic si[illegible]
close pr[illegible]
[illegible] proximal to it is usually large. In most instances the arterial pattern is normal but large, distended venous conglomerations are pathological and [illegible]

[illegible] very localised and are excessive
[illegible], however, the lesion is more proximal, and appears to affect a very



FIG. 159
Arteriogram of the lower limb just below the knee joint Patient with Buerger's Disease This shows a normal popliteal artery of good calibre with thrombosis at the level of the knee joint Extensive collateral vessels in the calf are shown with refilling of a short section of the posterior tibial artery through these collaterals

disease when there is isolated obstruction of the lower femoral and popliteal arteries, or where the patient with Buerger's disease has superimposed degenerative arterial disease.

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[illegible] the site may declare itself by the appearance of [illegible] case a second injection [illegible] carried out at the sus-[illegible]

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[illegible] can be very localised and are excessive [illegible] If, however, the lesion is more proximal, and appears to affect a very



Fig 160

Arteriogram of the hand In this case the radial artery was injected at the wrist joint A localised arterio-venous fistula was demonstrated in the middle finger A large number of rather tortuous, dilated veins are filling very rapidly after injection of the contrast medium



FIG. 161
Arteriogram of a patient with an extensive arterio-venous fistula above and below the knee joint. The femoral and popliteal arteries are clearly outlined and so is the conglomeration of rather tortuous venous channels just above and below the knee joint, demonstrating the extent of the arterio-venous communication.

large artery and vein, the number of venous channels is very excessive and may spread over a wide area (Fig. 161). In most cases arterio-venous communications are multiple and demonstration then is impossible. Because of an





FIG. 162 FIG. 163

FIG. 162 Arteriogram of the region of the knee. Lateral projection This shows the irregular popliteal artery which fills inadequately in its upper part

FIG. 163 Film taken of the same area as in Figure 162 within a second shows quite satisfactory filling of the aneurysm, demonstrating the delayed filling

excessive shunt of the contrast medium in the proximal lesion, inadequate amounts of contrast medium are retained in the circulation to demonstrate the peripheral communications, and it may be necessary to site the intra-arterial

injection at an unorthodox point, such as the popliteal or even the tibial artery in the lower limb, or the radial or ulnar artery in the upper limb. If a demonstration of the fistula by arteriography has failed resort may be made to retrograde venography, to outline the rather tortuous, dilated veins which will, to some extent, localise the lesion although it will not actually demonstrate the fistula.

ARTERIOGRAPHY IN THE DIAGNOSIS OF PERIPHERAL VASCULAR ANEURYSMS

Arteriographic demonstration of an aneurysm is important, not only for the diagnosis but also to predict the pathological situation likely to be found at operation.

TECHNIQUE.—The injection technique is identical with that carried out in the investigation of obliterative vascular disease. The radiographic technique, however, is slightly different. It is only necessary to obtain radiographs of the lesion and the vessels in its vicinity, and for this purpose it is important to obtain serial studies of the aneurysm, as filling of both the aneurysmal sac and the adjacent vessels may be delayed for considerable periods, and the demonstration of the actual anatomy may be missed on a single film. Three to four films, taken at a few seconds' intervals, are usually adequate for a complete and satisfactory demonstration of the pathological anatomy. The limb which is to be investigated is placed on a cassette tunnel of the same type used for peripheral arteriography, and by manual changing of the cassettes at the appropriate sites serial films can be obtained quite simply. If, however, they are multiple aneurysms, it may be necessary to extend the examination site over a wide area and the extent of the investigation will be pre-determined by the clinical findings. The injection for a popliteal aneurysm or an aneurysm in the tibial artery should be made in the femoral artery, below Poupart's ligament. For aneurysms of the arm, below the elbow joint, or in the region of the hand, the brachial artery is the site of choice. If the [illegible] part of the [illegible] is in an inaccessible or ab[illegible] be made to thoracic



FIG. 164
Traumatic popliteal aneurysm. A large, saccular aneurysm is demonstrated just above the knee joint.
(British Journal of Surgery.)

INTERPRETATION.—Irrespective of the aetiology of the aneurysm, an accurate anatomical demonstration of the sac is in most cases possible. Only if the aneurysmal sac is obliterated by thrombus or if the artery is blocked



FIG. 165

Aortogram. Multiple saccular aneurysms of varying size are demonstrated in the common and external iliac arteries

proximal to the aneurysm is an arteriographic demonstration of the lesion impossible. If the sac is only partly thrombosed or the aneurysmal neck relatively small, there can be considerable delay in filling and a satisfactory view of the anatomy will thus only be obtained by a study of serial films (Figs. 162 and 163). Saccular aneurysms, if post-traumatic or due to localised disease

of the artery, are usually smooth in outline (Fig 164). In degenerative arterial disease, however, fusiform dilatation or saccular aneurysms are usually irregular in outline, may be quite bizarre in appearance (Fig. 165) and are often



Fig 166

Arteriogram of the right hand Patient with primary Raynaud's phenomenon. This shows a perfectly normal arterial tree in the carpus and phalanges. Early venous filling

multiple. In the absence of extensive thrombosis of the aneurysmal sac or of the afferent artery, collaterals do not appear. If, however, there is a considerable block present in either site, collaterals develop and appear in the same way as in obliterative arterial disease.

INTERPRETATION.—Irrespective of the aetiology of the aneurysm, an accurate anatomical demonstration of the sac is in most cases possible. Only if the aneurysmal sac is obliterated by thrombus or if the artery is blocked

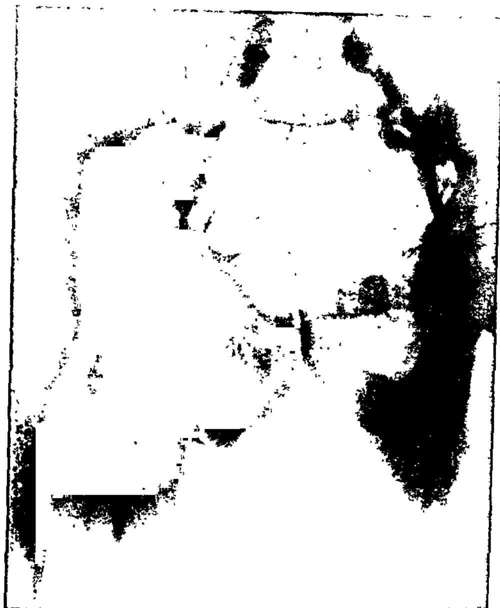


FIG. 165
Aortogram Multiple saccular aneurysms of varying size are demonstrated in the common and external iliac arteries.

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seen. The vascular supply to the fingers appears to be good and early venous filling on later serial films is constant (Fig. 166). The arterial calibre of the digital arteries may be very slightly diminished in some cases but an accurate



FIG. 168

[illegible]

assessment of the size of these arteries by arteriographic means is not practicable and no collateral vessels are outlined (Fig. 167).

In Raynaud's phenomenon, due to primary vascular disease, the arteriogram may be abnormal. It is usual to see minor arterial blocks and considerable narrowing, particularly of the carpal and digital vessels. The arterial blocks are often multiple and associated with a demonstrable collateral cir-

RAYNAUD'S PHENOMENON

In the diagnosis of Raynaud's phenomenon, arteriography plays an important part and the technical procedure is identical with that in degenerative arterial disease in the upper limb.



FIG. 167

Arteriogram of the hand Patient with *Raynaud's phenomenon* This shows good filling of the palmar and digital arteries. The digital arteries are of very small calibre

INTERPRETATION —In primary Raynaud's phenomenon, the appearances of the forearm, hand and digital vessels are normal. No obstruction can be

anaesthesia, just below and medial to the biceps tendon in the antecubital fossa A No 8 or 9 U S A. gauge radio-opaque cardiac catheter is then inserted into the artery and guided under fluoroscopic control to the appropriate position in the thoracic aorta. The right radial artery should be used when the injection is to be made into the ascending aorta and aortic arch since Broden[29] *et al.* (1949) found that the catheter, when passed up the left radial artery, enters more readily into the descending aorta.

This latter approach is of some use in aortography of the descending aorta and abdominal aorta. The optimum position for the tip of the cardiac catheter in the investigation of the ascending aorta is above the Sinus of Valsalva. Care must be taken that the catheter is not placed beyond this point, to avoid damage to the aortic cusps or entry of the catheter into the coronary arteries[23]

Arterial spasm sometimes gives rise to difficulties in inserting the catheter, but this is best overcome by rapid passage of the catheter or by local applications of 2·5 per cent. papaverine. The catheter usually passes along the brachial artery easily but its tip may be caught in some of the branches arising from the axillary and subclavian arteries. This is particularly prone to happen in coarctation of the aorta where these vessels have major collaterals. By raising the arm upwards or by pressing the hand firmly into the axilla, some of these difficulties may be overcome. The possibility of congenital anomalies must also be taken into account, and accurate positioning of the catheter tip under screen control is essential.[23] The contrast medium of choice is 50 per cent. diodone for coarctation and 70 per cent diodone for aneurysms and arterio-venous fistulae. Fifty to 60 cc. are used and the injection time should not exceed three to five seconds. This can be achieved with the aid of a pressure pump.[27] When the catheter is withdrawn after examination, an attempt should be made to reconstitute the radial artery, but if this is not feasible, the artery is ligated and tied without untoward effect.

RADIOGRAPHIC TECHNIQUE.—A manually or mechanically operated cassette changer must be used and it is preferable to [illegible]

[illegible]

tial. T [illegible] results will be obtained if the patient is placed on the radiographic couch and screened in position before the examination is carried out, and if the patient has to be moved on a trolley, skin marking for re-centering, of the radiographic field which is to be covered, is helpful.

COMPLICATIONS OF THORACIC AORTOGRAPHY.—If the examination is carried out under local anaesthesia there is a feeling of intense heat in the head and subsequently in the body, following shortly after the injection. There

culation. The filling of the terminal digital vessels and the vascular network of the pulp often cannot be demonstrated (Fig. 168). Venous filling on later serial films is nearly always absent, indicating a restricted vascular supply to the fingers. When assessing vascular filling of the digital vessels it is most important to differentiate streamlining from true obliteration and this can *only* be achieved if serial films are studied; streamlining disappears whereas true obliteration persists throughout the whole examination. One must also guard against misinterpretation of the appearances if the injection is made into the radial artery. As has already been mentioned, injection of contrast medium into the radial or ulnar arteries leads to *inadequate filling of the digital vessels* with contrast medium in the opposite tributary areas. It is therefore desirable, when the hand and digital vessels are to be demonstrated, that the injection should be made into the brachial artery just at the elbow joint.

AORTOGRAPHY

INTRODUCTION.—Radiographic demonstration of the human abdominal aorta was first accomplished by Dos Santos[23] and his colleagues in 1929. The thoracic aorta was first outlined radiographically by Castellanos and Pereiras[24] in 1939 by retrograde injection of contrast medium through the axillary and brachial arteries. Since aortography has become possible, many varied techniques have been developed and the scope of the examination greatly widened, particularly in the investigation of peripheral vascular disease and vascular pathology of the abdominal viscera. For the purposes of the discussion of technique and interpretation, it is convenient to divide the investigation into thoracic and abdominal aortography and to describe each separately.

THORACIC AORTOGRAPHY

INDICATIONS.—(1) In coarctation of the aorta, when venous angiocardiography has failed to give adequate information; (2) in the differential diagnosis of aneurysms from other mediastinal shadows; (3) in the accurate anatomical diagnosis of aneurysms, as a pre-operative measure; (4) in the localisation of arterio-venous fistulae; and (5) to outline the large vessels in the upper mediastinum, such as the innominate, carotid or subclavian, if vascular pathology is suspected in these regions.

TECHNIQUE.—Direct puncture of the thoracic aorta through the second intercostal space was carried out by Radner[25] in 1945 and by Meneses Hoyos[26] in 1948, but this method has not found general acceptance because of its potential danger. Jonsson[27] in 1949 first described percutaneous puncture of the carotid by cannula and retrograde injection into the aorta by this route and Broden *et al.*[28] in 1948 described retrograde catheterisation of the aorta via the radial artery, and it is this method which has become firmly established and is most commonly used today. The radial artery is exposed under general

anaesthesia, just below and medial to the biceps tendon in the antecubital fossa A No 8 or 9 U.S.A. gauge radio-opaque cardiac catheter is then inserted into the artery and guided under fluoroscopic control to the appropriate position in the thoracic aorta. The right radial artery should be used when the injection is to be made into the ascending aorta and aortic arch since Broden[27] *et al.* (1949) found that the catheter, when passed up the left radial artery, enters more readily into the descending aorta.

This latter approach is of some use in aortography of the descending aorta and abdominal aorta. The optimum position for the tip of the cardiac catheter in the investigation of the ascending aorta is above the Sinus of Valsalva. Care must be taken that the catheter is not placed beyond this point, to avoid damage to the aortic cusps or entry of the catheter into the coronary arteries.[29]

Arterial spasm sometimes gives rise to difficulties in inserting the catheter, but this is best overcome by rapid passage of the catheter or by local applications of 2·5 per cent papaverine. The catheter usually passes along the brachial artery easily but its tip may be caught in some of the branches arising from the axillary and subclavian arteries. This is particularly prone to happen in coarctation of the aorta where these vessels have major collaterals. By raising the arm upwards or by pressing the hand firmly into the axilla, some of these difficulties may be overcome. The possibility of congenital anomalies must also be taken into account, and accurate positioning of the catheter tip under screen control is essential[29] The contrast medium of choice is 50 per cent. diodone for coarctation and 70 per cent diodone for aneurysms and arterio-venous fistulae. Fifty to 60 cc. are used and the injection time should not exceed three to five seconds This can be achieved with the aid of a pressure pump[27] When the [illegible]
after [illegible]

[illegible]RADIOGRAPHIC TECHNIQUE.—A manually or mechanically operated cassette changer must be used and it is preferable to carry out the examination in two planes simultaneously. This is certainly [illegible]
and [illegible]

[illegible] are not essential
say, two to three seconds, u[illegible] cassette tunnel, will give the necessary information Accurate positioning of the patient for either method is essential. The most satisfactory results will be obtained if the patient is placed on the radiographic couch and screened in position before the examination is carried out, and if the patient has to be [illegible]
re-centering, of the radic[illegible]

COMPLICATIONS OF THORACIC AORTOGRAPHY.—If the examination is carried out under local anaesthesia there is a feeling of intense heat in the head and subsequently in the body, following shortly after the injection. There

is a slight increase in the pulse rate and a drop in the blood pressure. A not inconsiderable amount of the contrast medium in aortography of the thoracic aorta passes through the carotid arteries into the cerebral circulation and may give rise to cerebral arterial damage.

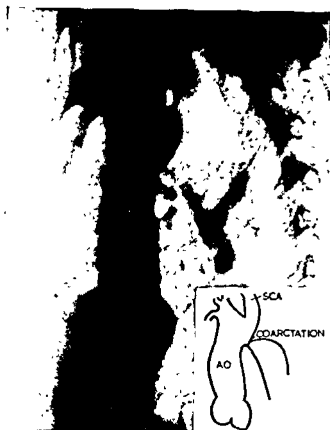


FIG. 169
Aortogram by aortic catheterisation, oblique projection Patient with coarctation of the aorta. The site and type of the coarctation is clearly demonstrated and so are some of the collaterals in the upper mediastinum SCA = Subclavian artery. AO = Aorta.
(*British Journal of Radiology*)

In one of Broden's patients[29] some of the contrast medium was injected by mistake into the innominate artery and this caused epileptiform attacks. The symptoms, however, were transient and these attacks passed off within a few days. But even when the injection is made into the aorta the risk of cerebral complications must be kept in mind. Signs of brain damage producing epileptiform spasms have been observed in cerebral angiography.[30] Such complications occurred particularly in epileptics and in patients with hypertension Broman and Olsson[31] have shown in an experimental study that brain damage can be produced by injections of a high concentration of diodrast into the carotid arteries of rabbits. Broden *et al.*[29] have used 70 per cent. diodone in

a large number of their investigations for coarctation of the aorta but latterly have accepted 50 per cent. in view of the danger to the cerebral vessels with the higher concentrations; they have found that the lower concentration gave adequate and satisfactory results.



FIG 170
Venous angiogram - lateral projection Patient with an aneurysm of the thoracic aorta The contrast medium clearly outlines the double aneurysm in the thoracic aorta

(a) *Interpretation.*—In coarctation of the aorta, the aortogram demonstrates with accuracy the site and extent of the lesion and the relationship of the main vessels in the upper mediastinum to the coarcted segment of the aorta, the state of the aorta above and below this narrowed segment and the presence of other anomalies, such as patent ductus arteriosus or aneurysms arising from the aorta or collateral vessels (Fig 169). Operability and the type of opera-

tion to be performed will, to some extent, depend on the radiographic findings If the coarcted segment is very extensive or an aneurysm is present near the site of the coarctation, a graft may be necessary. If the coarctation is very close to the subclavian artery, or, in fact, involves the subclavian, special technique may be required.

(*b*) *Aneurysms of the aorta.*—With the aid of aortography it is possible to outline aneurysms, either of the aorta itself or of its major branches within the mediastinum, and thus differentiate them from other mediastinal tumours which, on the plain film, may simulate such an aneurysm. An exact differential diagnosis is necessary, particularly as a pre-operative measure (Fig. 170).

(*c*) *Arterio-venous fistulae.*—In fistulae involving either the aorta or the major vessels arising from the aorta, aortography may outline the fistula and its extent. This may be of help if the diagnosis is obscure, or as a pre-operative measure if the fistula is to be closed or resected.

Abdominal aortography.—In 1929,[23] Dos Santos *et al.* described the trans-lumbar technique of aortography and the demonstration of the abdominal aorta and its branches, as well as the arteries of the pelvis and lower extremities. Basically the method has not changed since its first description but only with the advent in later years of good and safe contrast media did the examination become established procedure. The method was at first used as a diagnostic aid in the investigation of renal disorders and abdominal tumours, and within a short period many accounts dealing with the original experiences appeared in the literature. Nelson[32] (1945), Doss[33] (1946), and Wagner[34] (1947) simplified the original Dos Santos technique and widened its scope to include the investigation of general vascular disorders Leriche[35] applied the method in an extensive investigation of intrinsic diseases of the aorta and iliac vessels. A large series of examinations in an investigation of renal and vascular disorders was reported by Goodwin[36] in 1950, Griffiths[37] in 1950, Sante[38] in 1951, Detterling[39] in 1952, and these authors clearly show the value of the method and its practical application.

INDICATIONS.—(1) In obliterative arterial disease affecting the aorta and iliac vessels; (2) in aneurysms and arterio-venous fistulae for diagnostic purposes or as a pre-operative measure; (3) in certain urological conditions.

TECHNIQUE.—The examination is carried out under general anaesthesia. The patient lies prone on a cassette tunnel and his position is so adjusted that either a 15″ x 12″ cassette or a 14″ x 17″ cassette which has been placed in the tunnel covers the abdomen from the diaphragm down to the symphysis pubis. The aorta is approached by the lumbar route using a 6″ 16G. needle. It should carry a two-way tap, one opening of which is connected to a syringe containing heparin saline, and the other to the contrast medium. The needle is inserted a hand's breadth from the midline opposite the first lumbar vertebra and directed upwards and medially beneath the twelfth rib and then gradually advanced towards the twelfth dorsal vertebra Once the needle is felt to

impinge on the vertebral body, it is withdrawn slowly and further advanced less obliquely to slide past the edge of the vertebra. After it has been advanced approximately another two centimetres, the needle point is felt to enter the aorta. Immediately blood will be seen to stream back into the attached saline syringe The needle should then be advanced a further half a centimetre, to ensure that its point is well within the aortic lumen. The two-way adaptor is then switched over to the contrast medium. Fifty ml. of 70 per cent. Diodone are injected as rapidly as possible into the aorta. This should be done by an assistant, either manually or with the aid of a pressure device, similar to that mentioned for thoracic aortography. Occlusion of the lower limb circulation with a sphygmomanometer cuff is helpful in an investigation of renal disorders and abdominal tumours, but in peripheral vascular disease this should not be done.

RADIOGRAPHIC TECHNIQUE.—The cassette tunnel on which the patient lies should be fitted with a stationary Lysholm grid and then placed on to the radiographic couch. Before the examination is carried out, a preliminary radiograph must be taken to confirm the correct position of the patient. For the actual examination three films are taken as rapidly as possible, the first being exposed after two-thirds of the contrast medium has been injected. The cassette is then changed, either mechanically or manually and the second film taken and this is repeated a third time. But even in the absence of a cassette tunnel, a single film taken at the optimum moment on a simple Potter Bucky couch will give satisfactory results. This exposure should be taken after two-thirds of the contrast medium has been injected.

An alternative method for abdominal aortography is by the retrograde approach, which in many ways is similar to the retrograde injection of the thoracic aorta Castellanos[40] (1939) obtained an abdom[illegible]

[illegible] femoral artery. The catheter was then threaded into the abdominal aorta and 70 per cent. diodrast injected under pressure. This method was further developed by Helmsworth[42] in 1950 and Peirce, E C.[43] (1951) who replaced the ureteric catheter by a polythene tube. The retrograde method is more cumbersome than direct puncture and it requires exposure of the femoral artery below Poupart's ligament with an incision of the vessel Intubation of the femoral artery with a cannula and retrograde intubation of the vessels by a polythene tube over a stilette is a further development of the original method of Castellanos and is now being practised in Scandinavia[44] The only [illegible]

[illegible] radiographic [illegible] are identical to the method used in

tion to be performed will, to some extent, depend on the radiographic findings. If the coarcted segment is very extensive or an aneurysm is present near the site of the coarctation, a graft may be necessary. If the coarctation is very close to the subclavian artery, or, in fact, involves the subclavian, special technique may be required.

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RADIOGRAPHIC TECHNIQUE.—The cassette tunnel on which the patient lies should be fitted with a stationary Lysholm grid and then placed on to the radiographic couch. Before the examination is carried out, a preliminary radiograph must be taken to confirm the correct position of the patient. For the actual examination three films are taken as rapidly as possible, the first being exposed after two-thirds of the contrast medium has been injected. The cassette is then changed, either mechanically or manually and the second film taken and this is repeated a third time. But even in the absence of a cassette tunnel, a single film taken at the optimum moment on a simple Potter Bucky couch will give satisfactory results This exposure should be taken after two-thirds of the contrast medium has been injected.

An alternative method for abdominal aortography is by the retrograde approach, which in many ways is similar to the retrograde injection of the thoracic aorta. Castellanos[40] (1939) obtained an abdominal aortogram by retrograde injection of the femoral artery. His technique was further improved and modified by Farinas[41] (1941) who used the method for an extensive investigation of the abdominal aorta and its branches, in renal disorders, and in peripheral vascular disease. Farinas used a ureteric rubber catheter and introduced the catheter through a trochar in the femoral artery. The catheter was then threaded into the abdominal aorta and 70 per cent. diodrast injected under pressure. This method was further developed by Helmsworth[42] in 1950 and Peirce, E C[43] (1951) who replaced the ureteric catheter by a polythene tube. The retrograde method is more cumbersome than direct puncture and it requires exposure of the femoral artery below Poupart's ligament with an incision of the vessel Intubation of the femoral artery with a cannula and retrograde intubation of the vessels by a polythene tube over a stilette is a further development of the original method of Castellanos and is now being practised in Scandinavia[44] The only indication for the retrograde approach in abdominal aortography is in the investigation of abdominal *aneurysms* when *a direct* puncture is contra-indicated. The injection and the radiographic techniques in retrograde aortography are identical to the method used in

abdominal aortography by direct puncture but as a preliminary measure accurate positioning of the catheter within the aortic lumen under fluoroscopic



FIG. 171
Aortogram. Patient with atherosclerosis and inequality of femoral pulses This shows the extensive atheromatous changes of the right common iliac artery, producing marked filling defects in the vessel lumen Note the rather tortuous and irregular contour of the iliac vessels on both sides

control is essential. The tip of the catheter must be so placed that it lies well above the area which is to be investigated so that the contrast medium will enter the aortic lumen above the site under investigation.

1. Interpretation —In obliterative arterial disease, atheromatous changes in the aorta and iliac arteries are clearly demonstrated and so are partial and total blocks in any one of these vessels (Fig. 171). Total obliteration



Fig. 172

Aortogram Patient with atherosclerosis with absent pulses in the right leg and intermittent claudication This demonstrates thrombosis of the right common iliac artery just distal to the bifurcation

of the abdominal aorta ...
region of th...
the iliac vess...

... appearances were originally

abdominal aortography by direct puncture but as a preliminary measure accurate positioning of the catheter within the aortic lumen under fluoroscopic



FIG. 171

Aortogram Patient with atherosclerosis and inequality of femoral pulses. This shows the extensive atheromatous changes of the right common iliac artery, producing marked filling defects in the vessel lumen Note the rather tortuous and irregular contour of the iliac vessels on both sides.

control is essential. The tip of the catheter must be so placed that it lies well above the area which is to be investigated so that the contrast medium will enter the aortic lumen above the site under investigation.

artery. If the block is total, and in addition one or both common iliac arteries are involved, the circulation will be established through the small branches of the aorta, some retro-peritoneal arteries and, again, the inferior mesenteric

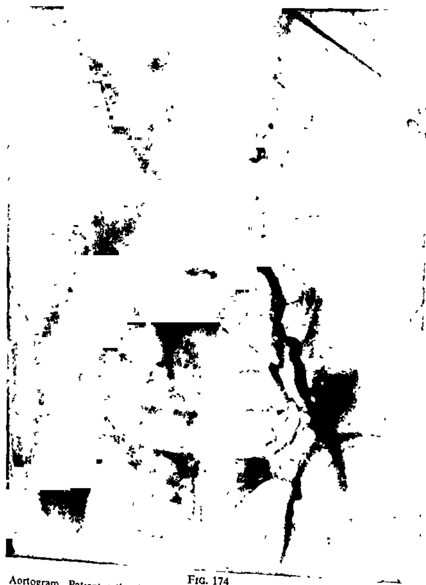


FIG. 174

Aortogram Patient with atherosclerosis and absent pulses right femoral artery. This shows good filling of the aorta, left common and external iliac and the femoral arteries The right side is not filled

(Fig 173). If the block is in the internal iliac artery, a very good collateral circulation can be established through the external iliac, perineal, gluteal, and obturator vessels (Figs. 174 and 175).

described by Leriche who discusses his experiences in a large series in 1952.[6] These findings and the degree of atheroma are of great importance if surgical

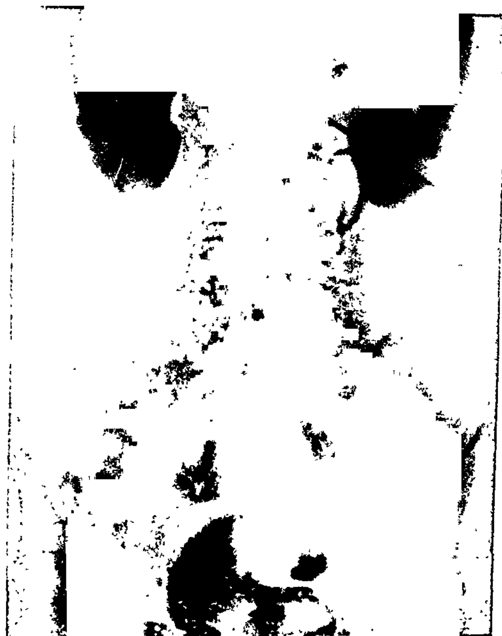


FIG. 173
Aortogram. Patient with atherosclerosis and absent pulses in both lower limbs. This shows a total block of the aorta just below the renal arteries. Extensive lumbar and pelvic collaterals are demonstrated

intervention is contemplated. They also give a good indication of the state of the collateral circulation which is of help in evaluating the prognosis and in estimating the results of lumbar sympathectomy.

If the aorta is blocked for a short distance below the renal arteries a fairly good collateral circulation will be established through the inferior mesenteric

2. ARTERIO-VENOUS FISTULAE.—The accuracy of this demonstration will depend largely upon the size of the fistula. If it is localised, arteriography



FIG. 176

Aortogram Patient with post-... This show ... hip joints

will be of help but if it is diffuse and wide-spread, it may be impossible to get an accurate demonstration (Fig. 176).

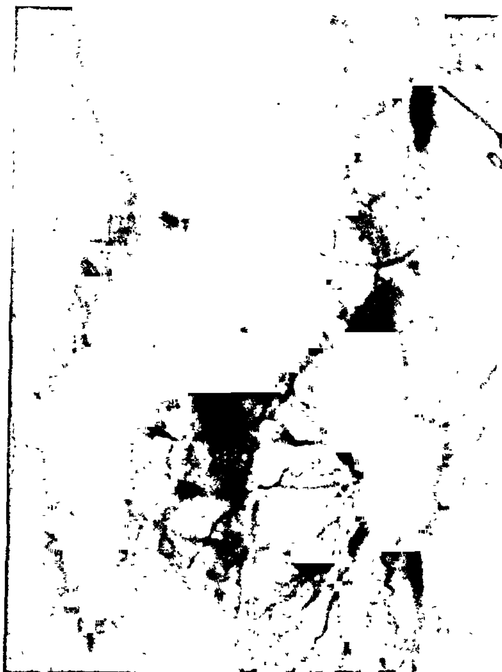


FIG. 175
Same patient as Figure 174. Films taken three seconds later show adequate filling of the right external iliac and femoral arteries through extensive collaterals in the pelvis. Both iliac arteries are very atheromatous

4. IN CERTAIN UROLOGICAL DISORDERS the aortogram is of value to demonstrate anomalies of the renal arteries and it can clearly show displacement of the renal anatomy by space-occupying lesions. It also helps to differentiate vascular from non-vascular conditions. In a differentiation of renal from other abdominal masses, the aortogram is of use as it demonstrates the circulation to the tumour very clearly. In some urological clinics this method of investigation is now routine practice. A large series have been reported by Griffiths[37] (1950), Doss[46] in 1951 and by Weyde[47] in 1952.

Contra-indications to aortography.—Iodine sensitivity or sensitivity to contrast medium are definite contra-indications but, as has been stated previously (p. 260), de-sensitisation of the patient is possible and after this has been done the examination can be carried out without ill effects. If there is seriously impaired renal or liver function the examination should not be undertaken, as large quantities of the highly-concentrated contrast medium may further damage these organs. Extensive calcification of a normal size aorta is in itself no contra-indication and we have had no serious haemorrhage from this. If there is fear of rupturing an aneurysm, aortography by the lumbar route is contra-indicated and the examination should be carried out by the retrograde method Severe deformities of the spine with secondary arthritis may make a puncture difficult, due to the difficulty of positioning the patient, and in these cases the retrograde method of injection is preferable.

Complications.—Peri-vascular injections can give rise to pain which may last up to twenty-four hours. In one of our patients, para-aortic injection produced an ileus Injury to the aortic wall and haemotoma formation can ensue but in our experience little trouble has been caused by this. Precipitation of a thrombosis in a distal vessel is a danger, particularly in obliterative arterial disease. If this is severe examination should only be carried out as a preliminary to surgery when 50 per cent. rather than 70 per cent. diodone should be used, as precipitation of thrombosis is more likely to follow after an injection of super-saturated 70 per cent. solutions Introduced by the lumbar route, the needle may enter the renal artery and the injection will be carried straight into this vessel No ill effects from this have so far been reported. We had this experience once and the injection was uneventful. In another case pneumothorax was induced by pleural puncture [illegible]

In thoracic aortography, damage to the cerebral arteries and coronary ischaemia have been noted if a too high concentration of the contrast medium reaches these vessels, and for this reason a meticulous technique and strict adherence to all the important points of the injection method, the placing of the catheter and a wise choice in contrast medium is absolutely imperative.

3. ANEURYSMS of the abdominal aorta will show up clearly on the aortogram. The extent and degree of involvement of important abdominal arterial branches is also shown (Fig. 177). The investigation is essential as a pre-

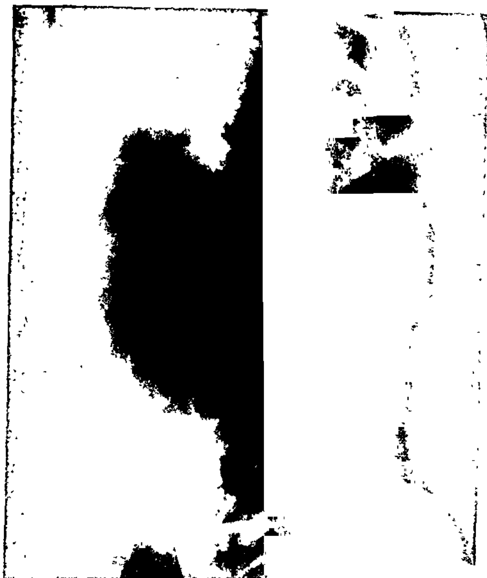


FIG. 177
Retrograde aortogram Patient with an aneurysm of the abdominal aorta The catheter has been threaded via the profunda femoris into the abdominal aorta and the tip placed at the level of D 12 A rather fusiform aneurysm is clearly outlined which extends above the renal arteries

operative measure. If, for instance, the aneurysm involves the renal arteries and coeliac axis and is too extensive, resection may be impossible. The investigation will also give some information about the state of the aorta above and below the aneurysm, since extensive atheroma may make surgical resection impossible.

saphenous opening in the groin in order to achieve adequate filling of the deep venous system.

From this brief description of the various views held by different authors it is quite clear that the situation is still very confusing and it is proposed only to describe the methods of Dow and Gryspeerdt, both of which in the author's view give reliable and satisfactory results.

After careful consideration, Dow in 1951 concluded that no one method previously described was entirely satisfactory, particularly in the investigation of pathological venous systems. Filling of all the deep veins was not always achieved and there was often only partial and irregular filling of normal veins It was thus impossible to differentiate non-filling due to thrombosis from non-filling due to faulty technique.

By using a tourniquet at the ankle joint or one at the ankle joint and one above the knee, filling of the superficial and deep venous systems in normal veins was in most instances satisfactory, at least from the ankle to the groin.

Radiographic technique.—For the procedure of venography the patient's limb is placed in the supine position on a cassette tunnel. After the veins have been emptied of blood by elevation and application of a crepe bandage which extends from the ankle to the groin, two tourniquets are placed around the limb, one above the malleolus and one around the thigh just above the knee joint. They must be tight enough to obliterate the flow in the superficial venous system. The contrast medium is then injected into an easily visible vein preferably on the lateral aspect of the foot, and before the injection is carried out the foot should be slightly elevated to avoid obliteration of the veins behind the malleolus due to pressure of the foot on the cassette tunnel.

After 15 to 20 cc. of 35 per cent. Diodone have been injected, the first film is exposed which covers the limb from the ankle to the knee, using a 15″ × 12″ cassette A further 15 cc. are injected up to a total of 30 cc. and two more films are exposed which again cover the limb from the ankle to above the knee joint The tourniquet above the knee joint is then loosened and further films are exposed to cover the region above and below the knee. By this time the last film has been exposed, the injection is completed and the procedure, from beginning to end of the injection and the exposure of the final film should not take more than thirty seconds. With this method Dow succeeded in the majority of cases in demonstrating satisfactory filling of the deep veins in the limb and to show their patency or possible obliteration. Gryspeerdt, in 1953, based his method on Dow's original procedure and described a few important modifications which gave even better and more constant results. The patient lies supine on an X-ray tilting table in a foot down position, with a 15° tilt. The limb to be examined is held in external rotation with a small, soft pad under the heel and the film is placed on the Potter Bucky tray just below the calf, using a 15″ × 12″ cassette which covers the limb from malleolus to knee. A polythene tube is then inserted and tied into a small

PERIPHERAL VENOGRAPHY

The radiographic demonstration of peripheral veins or large central veins in the trunk can be achieved, as in the case of arteriography, by injecting contrast medium into the veins. The methods, however, and the radiographic techniques are somewhat different and the results often unreliable.

VENOGRAPHY OF THE LOWER LIMB

Venography of the lower limb was first carried out by Dos Santos in 1938 who used this method of investigation in the diagnosis of thrombophlebitis. Since then a large number of papers have appeared dealing with the subject. Bauer in 1940 used the method for the investigation of deep vein thrombosis and similar examinations were carried out by Docherty and Homans in 1940, Starr in 1942, Mark in 1943 and Lesser and Raider in 1943. Allen and Barker in 1946 reported on their wide experience of the usefulness of the procedure.

Dow in 1951 and 1952 analysed accurately the methods so far described and developed his own technique, and discussed in detail the value of the procedure in the investigation of thrombophlebitis and deep vein thrombosis. Gryspeerdt in 1953 carried the procedure farther and added yet another variant to the previously described techniques and so did Cockett in the same year.

It is not proposed to discuss all the various methods of venography but to describe the most useful procedures for any given circumstances which will give some information of value.

In an investigation of the lower limb veins it is the aim (1) to outline with contrast medium both superficial and deep venous systems, (2) to demonstrate the communicating system between these two, and (3) to show any abnormality in the veins such as obstruction by thrombosis or incompetence of valves. It is generally the deep veins, their valves, and sometimes their abnormal communications with the superficial veins which have to be investigated. To achieve satisfactory filling of all the veins it is important that the contrast medium should be injected as distally as possible; the site of choice is below the ankle joint into a vein on the dorsum of the foot. To force the contrast medium into the deep veins the superficial venous system must be partly obliterated just above the site of the injection and this is best done by the application of a rubber tourniquet. This point was made by Hellstein in 1942 and confirmed by Bauer in the same year. Mahorner in 1943, Allen in 1946 and Jenny in 1947 suggested that the injection could be made into any small vein of the foot with the tourniquet placed just above the knee joint, thus obliterating the superficial system. They claimed that with this method adequate filling of deep veins could be achieved. Welch (1942) and DeBakey (1943) preferred to obliterate the superficial venous system at the

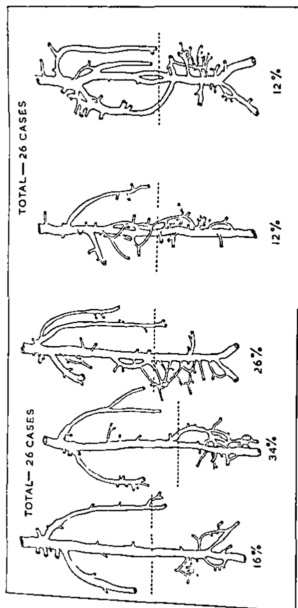


FIG. 178
Diagrammatic representation of the more common venous anomalies of the lower limb.
(After Gryspeerdt, *British Journal of Radiology*.)

vein on the dorsum of the foot through a skin incision about one centimetre in length. The advantage of using a polythene tube is to avoid leakages which so often occur through a skin puncture particularly when rapid injections of contrast medium are given. If the injection is to be rapid or if serial films are to be taken, this can easily be done with a polythene tube *in situ*. The catheter is kept patent by a saline drip to which should be connected a positive pressure infusion apparatus. One cc. of 35 per cent. Diodone is injected as a test dose and if there is no reaction, a rubber tourniquet is applied just above the ankle joint to occlude the superficial venous system. Forty cc. of 35 per cent. Diodone are then injected as rapidly as possible; after injection of about 15 cc. the patient is instructed to perform the Valsalva manoeuvre and the first film is exposed. The patient is then asked for a second time to carry out the Valsalva manoeuvre and after a further two or three seconds another film is exposed which covers the area of the knee and thigh. The patient then relaxes and the tourniquet is released. After the first examination the patient is turned into the lateral position and another 20 cc. of 50 per cent. Diodone are slowly injected over one minute. One minute after the end of the injection the Valsalva manoeuvre is again carried out and a film is exposed with the tube centred over the popliteal fossa. It is important that the patient should be instructed accurately in the performance of the Valsalva manoeuvre and a few trial attempts prior to the examination will be of considerable help.

Although with Gryspeerdt's method in the antero-posterior examination a fairly large quantity of contrast medium is injected at speed, no serious reaction will be encountered provided the patient is not sensitive to Diodone and apart from a feeling of flushing and sensation of heat there will be no unpleasant reaction. If only the deep veins are to be studied a crepe bandage must be applied from ankle to groin after the limb has been emptied of blood, in addition to the tourniquet above the ankle joint. A second tourniquet is placed above the knee joint to occlude the superficial veins satisfactorily. As an alternative to the Potter Bucky technique a cassette tunnel can be used, as described by Dow. This is placed under the limb and extends from groin to toes. By observing the technique previously described up to six films can be exposed at fairly rapid intervals, within half-a-minute, to cover filling of deep and superficial systems throughout the entire length of the limb.

In the lateral examination, injection of a smaller quantity of contrast medium is much slower and although there is some loss of contrast medium into the superficial system due to gravitation, this is not a serious drawback and satisfactory demonstration of the deep veins can be achieved sixty to ninety seconds after the injection has commenced. The Valsalva manoeuvre is of great help if carried out judiciously as not only will it retain the contrast medium for a fairly long time in the veins which are to be examined, but it will also help to demonstrate competent valves and help to fill the communicating veins between the deep and superficial systems. A considerable degree of retrograde flow will also be encountered which will aid in mixing the

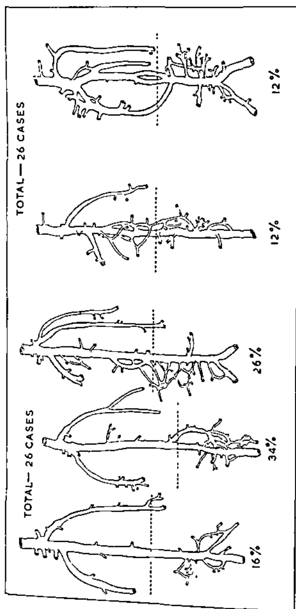


Fig. 178

Diagrammatic representation of the more common venous anomalies of the lower limb (After Gryspeerdt, *British Journal of Radiology*)



FIG. 179
Venogram of the lower limb which shows very clearly the popliteal and femoral vein as well as the saphenous vein and a number of communicating veins between these two systems



FIG 180
Venogram of the lower limb This shows a deep vein thrombosis in the calf and in the thigh just above the knee joint The popliteal vein has filled partly through collaterals via the saphenous system

contrast medium intimately with the blood in the venous systems, provided exposure of the films is delayed sufficiently and time is given for the valves



FIG 181
Venogram of the lower limb Deep vein thrombosis in the calf is demonstrated Only the superficial veins are outlined They are very numerous and dilated and pursue a tortuous course

to close if they are competent. Without the Valsalva technique actual valve competence cannot be assessed as the demonstration of valves is so often unsatisfactory and adequate filling of the para-valvular sinuses is impossible.



FIG. 182

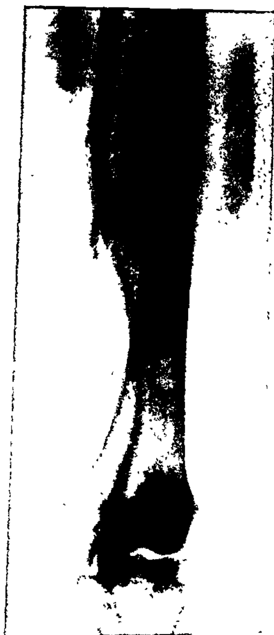


FIG 183

FIG. 182. Extensive varicose veins in the calf The deep veins appear to be patent
FIG 183 Retrograde venography shows good retrograde flow against the stream although there is evidence of functioning valves.

For the demonstration of the communicating veins, particularly above the ankle joint, the method described by Cockett is probably the most reliable. 20-25 cc of 50 per cent. Diodone are slowly injected into a small vein on the dorsum of the foot with the patient standing. No tourniquets are applied and the first film is exposed about thirty seconds after the start of the injection. A 15" × 12" cassette is used which covers the foot and calf up to the knee joint. In view of the erect position the contrast medium is held up by gravity in the [illegible] particularly above and behind the internal malleolus, the most important ulcer-bearing area.

Interpretation.—Anatomical variations of the deep and superficial venous systems are frequent and the more important ones are clearly described by Gryspeerdt (Fig. 178), particularly the deep veins in the thigh and popliteal fossa as well as variations in the communicating veins between the two systems. With the method described it is possible, in most instances, to outline the superficial and deep veins in the lower limb (Fig. 179) in the popliteal region and the veins of the thigh, and not only to demonstrate anatomical variations but also to show the presence of deep vein thrombosis (Figs. 180 and 181), the degree of collateral circulation between the two venous systems and the presence of extensive varicosities (Fig. 182) But only with the method described by Cockett is it possible to outline satisfactorily the communicating veins below the knee joint. Retrograde venography is unreliable as Dow has shown that normal valves may not close unless the pressure is increased to the same level as that achieved with the Valsalva manoeuvre (Fig. 183). But by using Gryspeerdt's method of flooding the superficial and deep systems with a sufficiently large amount of contrast medium, successful filling of both these systems is nearly always obtained and the Valsalva manoeuvre will, in the majority of cases, successfully demonstrate competent valves.

Summary.—No single method exists which will outline satisfactorily the entire venous system of the lower limb and thus demonstrate the patency of deep, superficial and communicating veins. With the application of the various methods described, such as the tourniquets above and below the ankle joint or above and below the knee, or with the use of the Valsalva manoeuvre, a lot of useful information can be gained by simple venographic techniques which may be of some value in correlating the clinical findings with the underlying pathology. From the purely diagnostic point of view, however, venography has not a great deal to offer as the clinical findings will, in most instances, give adequate and satisfactory information about the management of the case It can be said of venography that the only reliable information which will be obtained is that a vein which has been outlined is definitely patent, but that non-filling or inadequate filling of a vein does not necessarily imply that the vein is thrombosed or otherwise pathological.

VENOGRAPHY OF THE UPPER LIMB

This is an unusual procedure and is only carried out if an accurate localisation of an obliterated vein, such as the subclavian or axillary vein, is required.

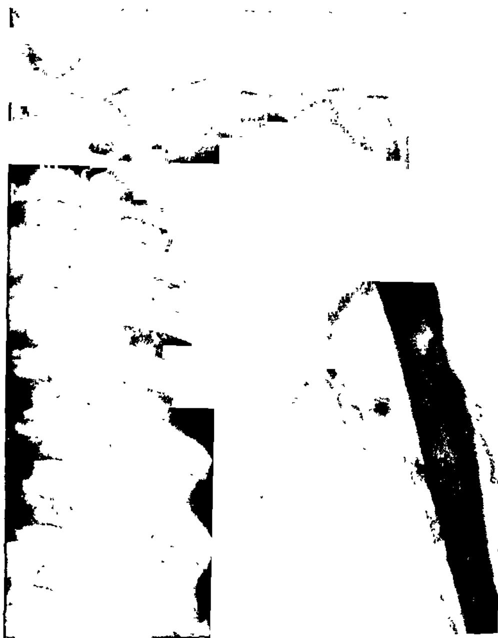


FIG. 184
Venogram of the upper limb Evidence of axillary vein thrombosis with collateral circulation around the shoulder

The patient lies supine on a radiographic couch or cassette tunnel. 20 cc. of 50 per cent. Diodone are injected slowly into an antecubital vein. After 15 cc. have been injected, *the first film is exposed which should* cover the



FIG 185

Venogram of the thoracic inlet. Patient with Ca. Bronchus and superior vena cava obstruction. Before radiotherapy. Thrombosis of the superior vena cava and an extensive collateral circulation at the root of the neck is demonstrated



FIG. 186

Same patient as Figure 185. *After* radiotherapy. The superior vena cava has partly recanalised. There is still, however, quite an extensive collateral circulation in the upper mediastinum and neck.

VENOGRAPHY OF THE UPPER LIMB

This is an unusual procedure and is only carried out if an accurate localisation of an obliterated vein, such as the subclavian or axillary vein, is required.

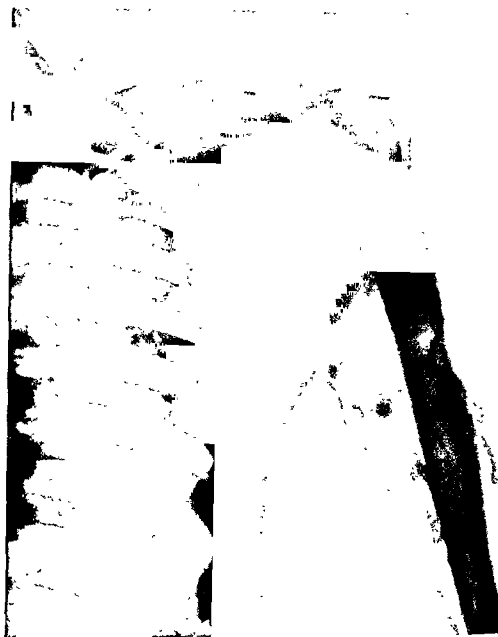


FIG. 184
Venogram of the upper limb Evidence of axillary vein thrombosis with collateral circulation around the shoulder

The patient lies supine on a radiographic couch or cassette tunnel. 20 cc. of 50 per cent. Diodone are injected slowly into an antecubital vein. After 15 cc. have been injected, the first film is exposed which should cover the

may thus be necessary to outline anomalous and extensive venous channels which are so often associated with congenital fistulae and this can often be

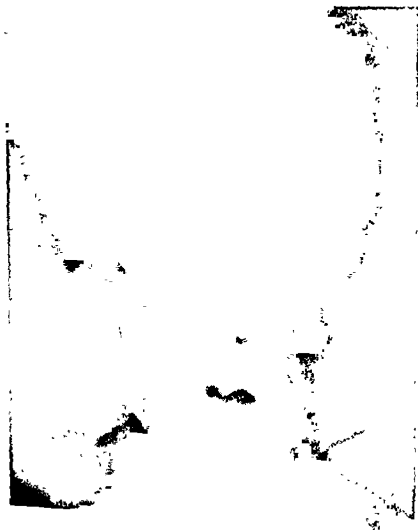


Fig 187
Venogram of the inferior vena cava. Patient with nephrotic syndrome and

done by retrograde venography. The limb to be examined is placed on a cassette tunnel and venography is done of the area under suspicion. It is

region of the shoulder and thoracic inlet and the second film is exposed towards the end of the injection. If more than two films are taken, a satisfactory demonstration of the collateral circulation around the shoulder, neck and thoracic inlet can be obtained (Fig. 184).

SUPERIOR VENA CAVA

The injection of contrast medium into an antecubital vein by direct puncture is not adequate and intubation of the subclavian or the superior vena cava itself with a polythene tube or cardiac catheter is necessary. The polythene tube is inserted into an antecubital vein, preferably a medial vein of the basilic group, so that the catheter can be introduced satisfactorily and without hindrance. If a lateral cephalic vein is used, the catheter is frequently held up over the shoulder in some of the smaller tributaries and satisfactory filling cannot be achieved. 40 - 50 cc. of 50 per cent. Diodone are injected as fast as possible and a number of films exposed at frequent intervals starting after half the amount of contrast medium has been injected. There should be a delay of two to three seconds between individual exposures of the radiographs. The cassettes should be placed so as to cover the thoracic inlet and upper chest. It is more satisfactory to use a cassette tunnel or a mechanical cassette changer than a Potter Bucky tray, and with this method a satisfactory demonstration of the superior vena cava and its tributaries can be obtained (Figs. 185 and 186).

INFERIOR VENA CAVA AND ILIAC VEINS

For the demonstration of the iliac veins and the inferior vena cava, a polythene tube should be introduced into one of the saphenous veins in the groin, threaded through the femoral vein and then tied in position. Up to 50 cc. of 50 per cent. Diodone are injected as rapidly as possible through the polythene tube. Four to six films are exposed at rapid intervals, the first being taken after half the contrast medium has been injected. To achieve rapid film changing, a cassette tunnel on which the patient has been placed is essential and the tube must be so centred as to cover the pelvis and abdomen. If retrograde filling of some of the caval tributaries, such as the renal or lumbar veins, is to be achieved, the patient should carry out the Valsalva manoeuvre starting at the beginning of the injection and holding it right up to the end, at which time one or preferably two films will have been taken. The patient is allowed to relax, only to start another Valsalva manoeuvre and is asked to hold on until two more films have been taken. With this procedure, very satisfactory retrograde filling of the renal veins can be achieved (Fig. 187)

ARTERIO-VENOUS FISTULAE

As has already been stated in the section on arteriography, demonstration of arterio-venous fistulae by the arterial route is not always satisfactory. It

may thus be necessary to outline anomalous and extensive venous channels which are so often associated with congenital fistulae and this can often be

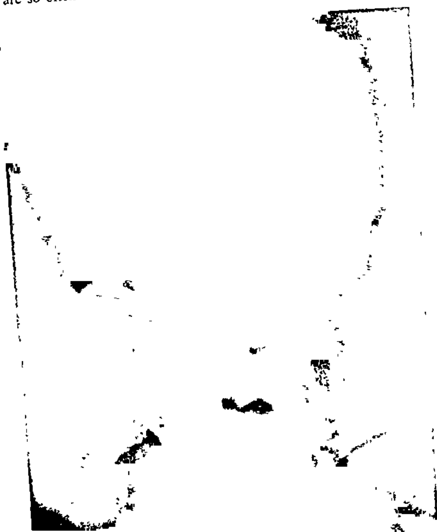


FIG. 187

Venogram of the inferior vena cava Patient with nephrotic syndrome and suspected renal vein thrombosis The left kidney has been removed in childhood The right common iliac vein, the inferior vena cava and two renal veins on the right side are demonstrated *Note*—Some of the contrast medium can be seen in the renal pelvis These appearances are due to an excretion pyelogram following injection of a test dose

done by retrograde venography. The limb to be examined is placed on a cassette tunnel and venography is done of the area under suspicion. It is

necessary to inject a large amount of contrast medium, 40 to 50 cc. of 50 per cent. Diodone, as rapidly as possible. After half the contrast medium has been injected, the patient is asked to induce a Valsalva manoeuvre and a number of films, up to three, are exposed at rapid intervals with the aid of a cassette tunnel or a mechanical cassette changer. It may thus be possible to outline extensive, anomalous venous channels in the region of the fistula and give some indication of the extent of the lesion.

R. E. S

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CHAPTER VII

THE PATHOLOGICAL PHYSIOLOGY OF PERIPHERAL ARTERIAL OBSTRUCTION

THERE is a significant difference clinically according to whether arterial obstruction is sudden or gradual in onset. Typically, sudden occlusion of the arteries occurs in embolism, and gradual occlusion in atherosclerosis. In the former emboli often lodge at the bifurcation of main vessels, but in the latter, narrowing occurs anywhere in the course of the larger vessels, and is in fact rather uncommon at their points of bifurcation. In either case obstruction is rendered complete by a super-added thrombosis. In many cases of embolism this may be rather extensive, blocking the origins of important branches both in the vessel primarily affected and in its distal branches, with consequently a severe ischaemia in a limb whose collateral vessels have not been utilised previously to any extent. On the other hand, where obstruction *is slow, as in atherosclerosis, the collaterals have gradually enlarged over a* long period in consequence of their use, and a super-added thrombosis has *frequently little further effect on the circulation of the limb. In certain* cases of thromboangiitis obliterans the severity of the symptoms of sudden ischaemia is intermediate between those resulting from embolism and atherosclerosis. This is so if the disease affects particularly the femoro-popliteal artery, so that this vessel, previously of normal calibre, is suddenly and completely obstructed by a thrombosis complicating a localised inflammatory lesion of the vessel wall.

THE COLLATERAL CIRCULATION

Some degree of arterial *obstruction* is *compatible with normal function of* a limb, and it frequently happens that an absent pulse is discovered accidentally on examination of the patient for some unrelated *condition. Similarly* at routine post-mortem examination some degree of arterial obstruction is *frequently found where there was no reason to suspect it* during life (p 337)

Alternate pathways for the blood exist but in the healthy person at rest they are of no great functional capacity, and a normal limb on arteriography shows little evidence of their presence (Fig. 188) Following narrowing or obstruction of a main vessel of a limb, the blood supply is maintained by these channels, which enlarge. These collateral vessels are not newly formed, but are the result of dilatation and enlargement of pre-existing vessels, and are more numerous and of larger capacity in the region of the joints where, *in the* healthy person, they are frequently called into use as a result of temporary obliteration *of the main artery on acute flexing of the joint.*

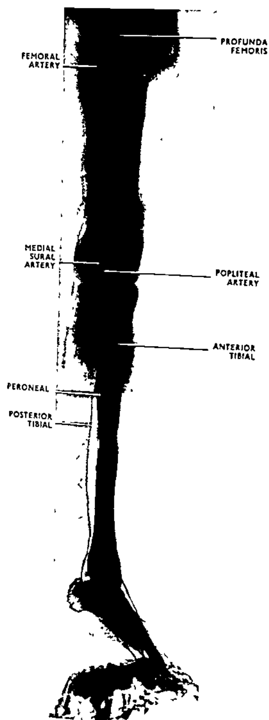


FIG. 188
Normal arteriogram of the lower limb



The collateral vessels arise from the main trunk, pass distally, in general parallel to it, and finally re-enter it beyond the obstruction, with the result that the vessel is refilled at a point as proximal as anatomical circumstances allow. In advanced cases of senile obliterative arterial disease, where there is extensive and often patchy obliteration of the main vessels, it appears to be a rule that any segment of such vessels that remains patent is filled by collateral channels, and such segments are often no more than a centimetre or so in length (Fig. 189). Thus, absence of filling of a main vessel as seen on arteriography indicates its obliteration

As regards the mechanism of the growth of the collateral circulation, this might occur as a result of three factors—nervous, metabolic or physical. A nervous factor can be discounted as a collateral circulation develops normally even though the central nervous pathways have been severed,[1] and in addition there is no evidence of afferent vasomotor pathways from the affected areas[2] Dilatation of collateral vessels from the local action of metabolites derived from the ischaemic tissues might be important but the circulation around an arteriovenous fistula continues to grow after amputation immediately distal to the fistula, and therefore after the removal of the site of origin of the metabolites.[3] There remains the physical factor As a result of obstruction in the main vessel there is a sharp fall in pressure in the artery distal to the block, with the result that there is a steep pressure gradient in the collateral vessels, communicating as they do with the main vessel above and below the obstruction. Von Recklinghausen (1883)[4] and Nothnagel (1889)[5] suggested this mechanism as the cause of the increased flow in the collateral vessels, and that this is probable has been confirmed by the behaviour of a model of a collateral system made of elastic rubber.[6]

In 1893 Thoma[7] stated his principle of vessel growth that " the increase in size of the lumen—is dependent on the rate of blood flow " In a narrow

FIG. 189 The main vessels are filled when they are patent

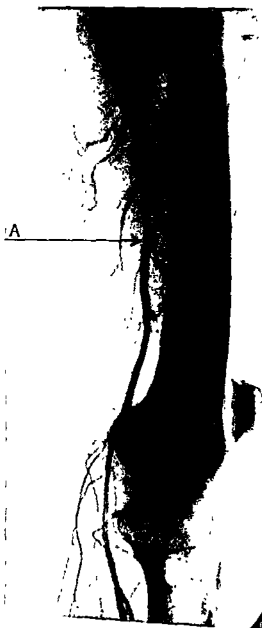


FIG. 190
Narrowing of the lumen at A is minimal, yet collateral vessels are beginning to be prominent



The collateral vessels arise from trunk, pass distally, in general parallel finally re-enter it beyond the obstructio result that the vessel is refilled at a proximal as anatomical circumstances advanced cases of senile obliterative arter where there is extensive and often patch tion of the main vessels, it appears to be any segment of such vessels that remain filled by collateral channels, and such seg often no more than a centimetre or so (Fig. 189). Thus, absence of filling of a m as seen on arteriography indicates its ob

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FIG 189 The main vessels are filled when they are pa

sympathectomy results in significant dilatation of collateral vessels following obstruction of a main vessel. It therefore appears that in sudden occlusion of the arteries there is a vasomotor factor interfering with dilatation of the



FIG 191
By-passing collaterals are present and functioning around the narrowed segment at A

collaterals and that experimentally and clinically dilatation can be immediately achieved by paralysis of the sympathetic nerves to the part by surgical or other methods[14] However, the degree of vasodilation achieved by sympathectomy in animals is no greater than that which would be achieved after some months if sympathectomy had not been done.[6] Therefore in animals

newly-utilised collateral, the blood-flow is rapid owing to the steep pressure gradient in the vessel, and as a result increase in capacity occurs, possibly as a result of increase of pressure on and stretching of the endothelial layer.[5] For some time the collaterals increase in size and often in length, the latter resulting in tortuosity. Longland[6] has recently demonstrated very convincingly by arteriography the development of collaterals in the rabbit.

The volume of flow through a tube varies with the fourth power of the diameter of the tube (Poiseuille's Law), and thus if the diameter of an artery is reduced by half, the blood-flow through that vessel is reduced sixteen-fold Therefore in gradual arterial obstruction blood-flow is reduced to such an extent that the collateral circulation is called on very early, a change that can frequently be seen on arteriography before obstruction is complete, and by the time the main vessel is completely blocked a remarkably adequate circulation has developed (Figs. 190 and 191). In 1868 Chiene[7] described the *case of a woman of sixty-five, who had died of paralysis, with a long-standing complete obliteration of the coeliac and both mesenteric arteries. The stomach,* liver, spleen, pancreas and duodenum had received their blood from the lower left intercostal arteries, the appendix and ascending colon from the lower right intercostal arteries, and the remainder of the intestinal tract from the superior haemorrhoidal artery, and the viscera all appeared normal.

The growth of healthy collateral vessels proceeds over a number of years, and if the original arterial obliteration occurred in youth and was the result of trauma rather than disease, the size of these vessels may be really *remarkable, and may be sufficient to supply the distal tissues* with an apparently normal amount of blood (Fig. 192). In adult life, it is during the first three months following arterial obliteration that the significant increase in their capacity occurs, though some further enlargement will continue for a year or more, and this is often manifest clinically by the gradual improvement of the symptom of intermittent claudication over the period of a year or more, although in some cases this results from re-education in avoiding the use of the painful muscles.

The collateral circulation is capable of functioning at very short notice and flow in these vessels is apparent very soon after abrupt obstruction of a main vessel Following digital obliteration of the femoral artery in the groin, blood flow in the calf muscles returns to its normal *resting* value in a few minutes,[10] and a faint pulse and small blood-flow has been demonstrated distally immediately after common femoral ligation.[11] Sometimes, however, sudden occlusion of an artery by an embolus, is followed by an initial period of delay in the establishment of a free collateral circulation, a delay which can be obviated by interruption of the vasomotor nerves to the part.[12] It has also been shown that *alcohol injection in the adventitia, at the same time* as the occlusion of the vessel with a paraffin embolus, induces greater circulation in a dog's limb so treated than in the control limb.[13] Longland (1953)[6] has demonstrated by direct measurement of the diameter of vessels visualised by arteriography that

sympathectomy merely accelerates maximum dilatation of collaterals. In man, however, even after years of ischaemia, sympathectomy still results in a surprising increase of blood-flow (p. 168).

Thus one or more segments of the main vessels may be very adequately by-passed, and the resting limb may not suffer from severe ischaemia, and if, as in atherosclerosis, the obstruction does not occur in the smallest arteries, the amount of blood reaching the distal part of the limb is generally sufficient to maintain life provided injury or sepsis is avoided.

Further decrease in the circulation, which may so reduce the blood-flow that gangrene is threatened, occurs from various causes:—

1. Involvement of the collateral vessels themselves by the disease—a rare phenomenon in atherosclerosis, but more frequent in thromboangiitis obliterans

2 Involvement of the origins of the collaterals from the main stem, a condition occurring frequently in atherosclerosis, whereby these vessels are constricted or "nipped" by disease in the wall of the parent vessel (Fig. 193), reproducing the familiar picture of atheromatous narrowing of the origins of the intercostal arteries from the aorta.

3 Spread of thrombosis in the main vessel, thus occluding the origins of many collateral vessels. This may occur from spread of disease in the main vessel, from intercurrent disease, particularly blood diseases, injury or operation, all of which may lead to some physico-chemical change in the blood, or to slowing of the blood stream from immobility, hypotension or shock

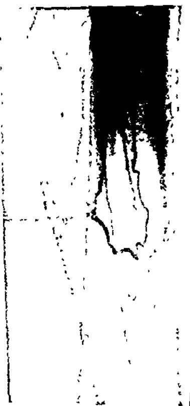


FIG. 193
The origin of the collateral is constricted by disease in the wall of the main vessel from which it arises

The longer the collateral channel, the more precarious i[illegible] with the length c[illegible] a tube varies Therefore obstru[illegible] its diameter. collateral channe[illegible] often tortuous [illegible] in serious embarrassment of the distal circulation

THE DISTRIBUTION OF THE DISEASE

Proximal disease.—The more proximal the obstruction the larger are the available collateral arteries and the more adequate is the collateral circula-



Fig. 192
Arteriogram of a man whose femoral artery had been tied in the lower part of Hunter's canal at the age of 14 He had no symptoms of ischaemia in the leg

the circulation and intravascular thrombosis. Venous thromboses, frequently seen in thromboangiitis obliterans, add to the inadequacy of the blood-flow. The severity of the ischaemia gives rise to pain and trophic changes, and ulceration and gangrene may occur spontaneously, although they are frequently precipitated by trauma. The colour changes in small vessel differ from those seen in main vessel obstruction. Rubor or cyanosis occur from



FIG 195
Atherosclerotic obstruction of the right internal iliac artery. There was a recent superadded thrombosis of the femoral, popliteal and more distal arteries Rubor was persistent in the right leg and did not change much with posture Pain was severe and diffuse. Amputation was done

extravasation of red cells and from engorgement of paralytically dilated capillaries, and the colour persists in spite of elevation or dependancy of the part, the blood in such vessels as are patent escaping with difficulty, and the circulation being almost stagnant (Fig. 194)

Colour changes which persist in spite of posture signify impending gangrene, and indicate a degree of arterial obstruction unlikely to be relieved by any vasodilating measures (Fig 195).

In atherosclerosis, when the obstruction is proximal, distal envolvement may occur:—

1 As a result of local thrombosis complicating sepsis or following trauma, mechanical, thermal or chemical.

2 As a result of thrombosis associated with sluggishness of the blood-flow due to advancing disease, recumbency during illness or after operations,

tion. Apart from intermittent claudication there may be few signs of distal ischaemia. Blood is *returned to the main vessels below the site of obstruction* and provided the distal vessels of the limb are patent, the amount of blood *reaching them is sufficient* to maintain the digits without pain or trophic change. The patency of the distal circulation *can be inferred from colour* changes occurring according to posture of the limbs. In the horizontal position *there is usually no* difference in colour between the healthy and the diseased limbs. On elevation pallor appears in the foot of the affected limb, and the



Fig. 194
Marked rubor of the phalanges with moderate rest pain in a patient with thromboangiitis obliterans. The pulses at the ankle joint were palpable. Rubor of the great toe persisted irrespective of posture. This toe was *amputated*

angle at which this appears is an indication of the severity of the arterial obstruction. When the pale limb is then allowed to become dependent, colour returns, but a delay of more than fifteen seconds indicates a moderate degree, *and of more than one minute a severe degree* of arterial obstruction. In long-standing cases and in those with a severe degree of arterial obstruction, rubor may later appear in the dependent foot and toes, due to paralysis of the capillaries from persistent anoxia. When the dependent limb is raised again, the rubor disappears rapidly, as though the blood was being poured out of the limb, *as indeed it is, the distal vessels being patent.*

Distal disease.—If the most distal vessels are obstructed, the collateral arteries are so small that blood-flow is insufficient for the tissues. Capillary anoxia and leakage of plasma and red cells *may lead to further interference* with

Swelling of an ischaemic limb.—This is always a sign of serious significance, and may occur:—

1. As a result of persistent dependancy, a position assumed by patients as it gives a measure of relief from rest pain
2. From capillary anoxia, resulting in increased permeability of these vessels
3. As a result of local sepsis.
4. After a deep venous thrombosis of the limb, rather a rare complication but a sinister one

Gangrene of a major part of a limb follows when a massive thrombosis of the main vessel occurs involving many of its branches It is more frequent when this is a sudden as opposed to a gradual process, as when an embolus is complicated by superadded thrombosis which spreads almost always in a distal direction It also occurs in a patient with atherosclerotic arteries who suffers from some complicating condition such as anaemia, polycythaemia vera, dehydration, shock, systemic infection or debilitating disease. Sometimes a massive thrombosis of a major vessel occurs without detectable cause.

P. M.

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and sometimes to the presence of increased coagulability of the blood from whatever cause, especially dehydration and polycythaemia.

3. As a result of emboli from proximal atheromatous plaques or intravascular thrombi, lodging in distal vessels.

The sequence of proximal arterial occlusion proceeding to distal occlusion, sepsis and gangrene is frequently illustrated by a patient with intermittent claudication who develops a black gangrenous toe as a result of an embolus. The toe is painless as it is dead, and adjacent tissues are relatively healthy right up to the gangrenous area, and are also painless and without any per-



FIG. 196
There is colour change persisting irrespective of posture There was a recent massive thrombosis added to a localised thrombosis in the femoral artery Amputation was done.

sistent colour change. Should sepsis intervene, then the adjacent part of the foot becomes painful and swelling appears with a redness which becomes persistent in spite of posture. Sepsis has led to local thrombosis of peripheral vessels, with resultant severe ischaemia of the tissues adjacent to the gangrenous part. It is instructive to note that a local amputation of a gangrenous toe where there is no pain, trophic change nor redness in the proximal tissues, is usually successful, whereas a local amputation done through painful, persistently ruborose tissue is rarely followed by healing (Fig. 196).

There are therefore two main varieties of arterial obstruction—the proximal type which is compensated by numerous collaterals, and the distal type where the smallest vessels of the extremity are affected, vessels which are not compensated by collaterals of significance, and such collaterals as there are, are often themselves diseased and obstructed.

it is of course possible for them to occur together and, since atherosclerosis is so widespread a disease, it is not surprising to find some of its lesions in those suffering from thromboangiitis, more especially in the older patients.

ATHEROSCLEROSIS

Aetiology.—We do not understand the exact cause of this condition though a number of factors are known to play a part. Moreover, there is still some uncertainty as to how the atheromatous lesion develops and until this matter is settled speculation as to its cause is hindered. For many years the teaching of Virchow, that the disease was a degenerative one in the intima, in which cholesterol-containing phagocytes appeared, to be followed by fibrous thickening of the sub-endothelial layer with related atrophic changes in the media, was generally accepted Recently, however, the whole matter has been called in question by Duguid,[1 2 3] who has revived Rokitansky's view that the atheromatous plaque is an "incrustation"—in other words a mural thrombus—which is laid down on the surface of the intima and becomes incorporated into the vessel wall. Duguid worked especially with the coronary arteries, but supporting evidence of the same kind in the aorta has come from his later papers and from Crawford and Levine.[4] Whilst it is not possible to discuss the details of the controversy here, we may say that Duguid does not claim that every atheromatous patch has at some time been a thrombus; and we would add that we ourselves would agree that it may be impossible to distinguish between a picture sometimes seen in an artery and known to result from thrombosis, from that believed to be simple atheroma. One difficulty in accepting the thrombosis view is to account for the great concentration of cholesterol and cholesterol esters in the depths of the patch. Clearly the quantity is too great to be derived from that initially present in a thrombus, so that some specific accumulation, or soaking in, must go on The same must also apply to the more conventional view of atheroma. This leads us to a question which has long exercised pathologists: the possibility that the cause of atheroma may lie in a disordered cholesterol metabolism Here again there is no clear answer. When atheroma-like lesions were found to be capable of being produced in the rabbit's aorta, by feeding the animal with cholesterol, the answer seemed found; but in the years which have passed since the original demonstration of this phenomena doubts have continued to grow as to whether this feeding has any real relationship to human atheroma. These are founded upon the very large quantities of cholesterol required, the unnatural nature of this substance to the rabbit's normal diet, the fact that cholesterol in such experiments also accumulated in large quantity in parenchymatous organs, as well as the lack of real similarity between the cholesterol masses deposited in the vessels, and elsewhere, and the picture of human atheroma On the other hand there is no escape from the chemical evidence of a great increase in cholesterol and cholesterol esters in the atheromatous aorta, and there is also some evidence that a high and sustained increase

CHAPTER VIII

THE PATHOLOGY OF ATHEROSCLEROSIS

GENERAL CONSIDERATIONS

THE observations and descriptions which are here given are in the main personal ones derived from the study of material provided by the amputation of limbs or toes on account of intolerable pain, or impending or actual gangrene. Some use has been made of excised portions of vessels, and in a few cases of post-mortem material, but for the greater part I have depended upon surgically amputated limbs. Hence my descriptions will be biased by a predominance of terminal stages. This bias may not, however, be as serious as might appear at first sight, since in a continuously progressing process early stages are to be found as well as late terminal ones in any given limb.

In an investigation which has been spread over fifteen years the general procedure has been to inject the arteries of the amputated specimen, as soon as possible after it has been received, with an oily radio-opaque medium* of a viscosity which prevents it from passing the capillaries, and by an immediate X-ray examination to obtain a picture of the arterial tree alone. There are technical difficulties about this procedure, the most obvious of which may be the occlusion by disease of the main vessel or vessels at the level of amputation. Where this has occurred a distal vessel, usually either the dorsalis pedis, or the posterior tibial behind the ankle, or both, has been opened and injection, if possible, made into these vessels in both peripheral and central directions. This same procedure of retrograde injection has also been used in some cases to amplify information obtained by a first injection at the amputation level

The information obtained from radiograms is of great value in making an initial assessment of the degree of alteration of the arterial tree and of its distribution It also serves another purpose for the pathologist in localising the sites from which it seems most profitable to take sections for histological examination. The whole process thus falls into three stages, injection and radiography, dissection guided by the information already obtained, and histological examination The observations made have been confined almost wholly to the disease in the leg as, except for an occasional finger amputation, the surgical operations which have provided my material have been upon the lower extremity, on which the incidence of ischaemic vascular disease falls with the greatest severity.

Chronic ischaemic disease of the lower limb is almost always the result either of atherosclerosis or of Buerger's disease. These are two distinct and different entities both from the clinical and pathological points of view, though

* The medium used by the writer consists of approximately 25 per cent metallic mercury in fine suspension in liquid paraffin

it is of course possible for them to occur together and, since atherosclerosis is so widespread a disease, it is not surprising to find some of its lesions in those suffering from thromboangiitis, more especially in the older patients.

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of these substances in the blood contributes to human atheroma. In subacute nephritis, with a high cholesterol content in the blood, atheromatous changes in the aorta and large vessels may be found in young subjects who normally would be free of such lesions, or only have them in a mild form. The same applies to diabetes; or did apply in the pre-insulin period in which a high fat diet was given and carbohydrate severely restricted. We shall note later that in our own series of atherosclerotic ischaemic legs no great difference has been found between the age incidence in diabetics and non-diabetics in later life, but a comparison made by others[5] points to the conclusion that the era of high fat diet was associated with a higher incidence of atherosclerosis, and that the disease occurred at an early age, when normally it should be absent.

A further, and old observation, is the relationship between local strain in the vessel wall and atheroma. There is general agreement that benign hypertension favours atheroma, but the best example of this effect is the development of the disease in the pulmonary artery, a vessel normally free from atheroma, in pulmonary hypertension.

In conclusion we may say that in our view too much stress has been laid on the presence of cholesterol and allied lipoid substances in the atheromatous lesion. All atheromatous lesions do not contain cholesterol deposits, and on the other hand the almost indistinguishable thickenings which result from thrombi may certainly come to contain them. Moreover, as regards the limb vessels, the lipoid infiltration of the atheromatous areas is much less in evidence than it is in the aorta or coronary arteries. It therefore seems likely that it may well be largely a secondary phenomenon, and that the lesions "imbibe" lipoids by some process which is not clear; though it is thought that it may be directly from the vessel's lumen. The occurrence of haemorrhage in the depths of atheromatous plaques which may precipitate thrombosis, especially in the coronary vessels, has been emphasised by Winternitz[6] and it certainly is a thing which may often be seen. We think this arises from the abnormal vascularisation of the sub-intimal tissues by the vasa vasorum, following the disruption of the internal elastic lamina which is associated with the advancing changes of atheroma in the intima. The presence of such haemorrhage has often been related to trauma,[7] which is rational if we believe it arises from a tearing of small vascular terminals supplying the depths of an atheromatous plaque, which lies as a rigid focus in the wall of a mobile tube.

THE SPECIAL PATHOLOGY OF ATHEROSCLEROSIS OF THE LOWER LIMB

This disease of the arteries is a penalty of advancing years. In the previous paragraph we have mentioned its earlier incidence, in the aorta especially, in certain diseases associated with hypercholesterolaemia. But in the writer's experience this does not appear to extend to the peripheral leg vessels in older patients. Thus in these series the average age at which amputation has been

required in diabetics (71·75 years) has not differed materially from that in those in whom there has been no diabetes (71 years), neither have there been any distinguishing pathological features between the two groups of cases.

The pathological changes in the arteries in atherosclerosis are associated to some extent with those usual in senility, and it is not always possible to say with any certainty where the physiological changes of senility end and the pathological ones of atherosclerosis begin. Intimal thickening,[8] in association with fibrosis of the media, is a concomitant of arterial ageing and since it is an essential feature in most examples of obliterative atherosclerosis the difficulty in making an absolute distinction is obvious.

Rodda,[9] working in the writer's laboratory, was able to distinguish senile intimal thickening, without atherosclerotic changes, in the arteries of the lower limb in forty-two out of fifty cases seen at routine post-mortems on subjects mostly over sixty years of age; nevertheless the distinction is not easy where atherosclerotic lesions are added to those of senility. The matter is not of great importance in the present connection since senile changes alone do not give rise to ischaemia. Rodda's investigation,[10] which did not extend higher than the upper popliteal artery, showed that there was no significant difference between the frequency of atheromatous intimal thickenings in the proximal and distal parts of the main vessels of the leg, though the proximal thickenings tended to be more necrotic and the distal ones more fibrotic Amongst such vessels the peroneal artery showed a little more freedom from pathological lesions than the others His survey did not include the profunda femoris artery, which is rarely found to be affected in arteriograms in the living.

The condition of Mönckeberg's sclerosis, or medial calcification, which is common in the elderly and often contributes to the sclerotic element in atherosclerosis, does not seem to be of much importance in the genesis of atherosclerotic ischaemia It is true that a rigid calcified media, in a limb vessel which may be required to provide an alternative route for the blood when another main vessel is occluded, may be thought to be a disadvantage by the physical limitation of its enlargement, but this effect is probably more theoretical than real, since the collateral circulation is usually carried on by vessels which are too small to be affected by medial calcification. Furthermore, medial calcification does not affect the intima and lead to thrombosis, which is so commonly present in atherosclerosis and is an important factor in the progress of the disease. It is well known to clinicians that there are certain sites of election for arterial obstruction, particularly the femoro-popliteal junction, the lower part of the popliteal, and the lower part of the posterior tibial In his series of asymptomatic cases Rodda found complete occlusion of some artery in 40 per cent. of all subjects, where the age exceeded sixty years. The greatest incidence of this was in the lower posterior tibial and lateral plantar arteries. The incidence of intimal thickening was greatest throughout the whole of the length of the popliteal artery, and in the upper part of the posterior tibial.

In chronic atherosclerotic ischaemia of severe degree all the changes of atheroma and fibrosis usual in the senile limb are encountered, but their incidence is higher and their severity much greater. Complete obliteration of

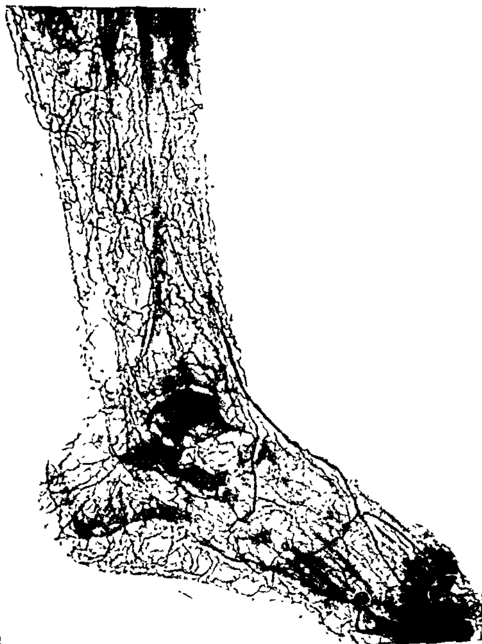


FIG. 197
Absence of all three main arterial trunks in the lower leg with good vascular pattern in the foot due to minor anastomoses

one or more of the main arterial trunks is usual (p. 340) and partial obliteration of these is often very extensive. The obliterative lesions vary very much in their severity and the amount of stenosis produced; they are usually wide-

spread and are never focal and, with the modification induced by the opening up of collateral channels, often produces an extreme distortion of the normal pattern of the arterial tree (for examples see p. 342 *et seq.*). At the same time, as we shall presently show, the lesions do not as a rule affect the smaller arteries of the extremity, including in this category the distal portion of the dorsalis pedis artery, the plantar arch, the plantar arteries, and the digital arteries (Fig 197). In general the more peripheral the vessels the less subject they are to chronic disease. The fault lies further back. Viewing the profound alterations of the main arteries it is sometimes difficult to conceive how a circulation to the foot has been maintained for so long The anatomical explanation lies in the arcade arrangement to which all the limb arteries contribute to some degree. The perfection of this system may be underestimated from a consideration of the ordinary anatomical diagrams which, except in such situations as the palmar arches or the messenteric rami, where the vessels are extended in a single plane, do not emphasise it. The effect, however, is that every considerable stretch of any limb artery may receive blood from more than one direction, and by secondary arcades as a rule from many directions; so that as long as there is a *vis a tergo* in a single limb vessel blood can, by anastomotic channels, fill isolated stretches in others which may be obliterated both proximally and distally. That the flow of blood in many of these diseased arteries runs in an opposite direction to the normal is shown by the fact that the vessels can in some cases only be injected by the retrograde route; in others most easily by this route It is also sometimes found that there is an arterial deformity in which a branch from an obstructed vessel forms a loop with its convexity directed proximally as shown in Figure 198: the explanation of this seems to be the effect of the pressure of blood flowing in a reverse direction. Further clinical evidence is that in amputations the surgeon may notice the blood spurting from the distal end of a severed artery. The arcade system, with its three dimensions, receives blood at a certain pressure (determined by the size of the vessels of ingress) and passes it forwards into the more peripheral terminals In the digits these lie at the extreme end of the arterial system, and though as a rule they are not themselves stenosed, and their supply is from the plantar arteries and the plantar arch—vessels which are often patulous—the latter receive their blood from the more proximal posterior and anterial tibial arteries which are frequently severely stenosed It follows that in such circumstances the circulation in the digits must be excessively stagnant, and anoxia well marked. From this are to be anticipated ischaemic pain, increased vascular permeability, oedema, local haemoconcentration with increased viscosity of the blood, stasis, and finally necrosis of tissue. In this way peripheral gangrene in areas with patent vessels is to be explained





FIG. 198

Sites and incidence of arterial obstruction in atherosclerotic ischaemia*

Occlusive disease, in cases in which it leads to amputation, almost always involves the complete obstruction of one or more of the leg arteries at several points. My own figures (classifying these vessels as: *femoro-popliteal, anterior tibial, posterior tibial* and *peroneal*), show that in approximately 6 per cent of cases one artery only was obliterated, in 45 per cent. two arteries, in 36 per cent. three arteries and in 15 per cent. all the vessels suffered complete occlusion somewhere along their course. A more detailed analysis of the sites and severity of occlusive lesions is shown in the following table and Figure 199.

TABLE IV

INCIDENCE OF CHRONIC OBSTRUCTIVE ATHEROSCLEROTIC LESIONS IN VESSELS OF THE LOWER LIMB IN CASES OF AMPUTATION FOR ISCHAEMIA OR GANGRENE

(per cent.)

	Feml	Popl	Ant Tib	Post Tib	Peroneal	Dor Ped	Ext Plantar	Int Plantar	Digitals
Obstructed	50	50	80	73	37	19	12	3	0
Partially obstructed	20	17	7	11	20	5	15	12	25
Patent	30	33	14	16	43	76	73	85	75

These are later figures than those given by the writer in the Ciba Foundation monograph (1) and are from a larger series.

These results emphasise the way in which the incidence of the disease falls upon the larger arterial trunks and the general way in which the distal small arteries, such as the intrinsic arteries of the foot escape. The exception in the larger vessels is the peroneal artery, which is as often as not unobstructed and is in consequence in many cases the main contributory channel to the circulation of the ischaemic limb. We shall revert to this fact later (p 354) What factors aid this relative immunity are not known. We may, however, point to the more direct course of this vessel and its relatively deep and protected position and long intramuscular course, and to the fact that it represents the primitive axial artery of the foetus.

Whether the different incidence of these arterial occlusive lesions reflects the date of onset of disease in the various arteries is uncertain Clinical evidence suggests that the posterior tibial is usually affected first and this the

* The reader is referred also to the important paper by A Lindbøm,[4] who has covered much of the same ground as the author on the living and the cadaver but with a more radiological bias and with more consideration of the thigh vessels and less of the peripheral vessels thus our work to some extent complements that of the other

above figures would support, though there is little difference between this and the anterior tibial On anatomical grounds the former is the more important artery of supply to the foot and therefore disease in it might be expected to produce the earliest clinical signs. Rodda, in his symptomless cases of sclerosis in the lower limb arteries, found the highest incidence of obliteration in this vessel

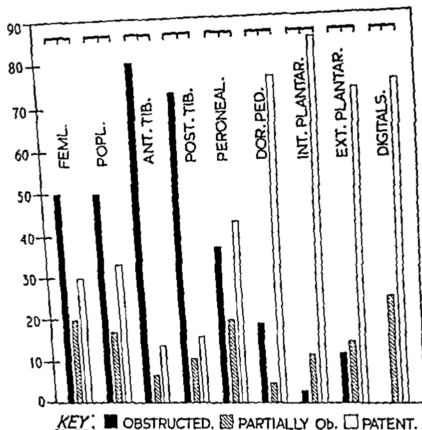


Fig. 199

Percentage incidence of chronic obstructive atherosclerotic arterial lesions (*see* Table IV)

Amongst these main arterial trunks the effects of obstructive lesions cannot be said to follow any regular pattern, but to lead to an almost infinite variety of pictures. As however the anastomotic channels available as an alternative course for the circulation when it is blocked are, as we shall mention later, to some extent pre-determined, certain features tend to repeat themselves. Since it is not practicable to give detailed descriptions of a large number of cases we shall confine ourselves to illustrate the changes by citing three examples.

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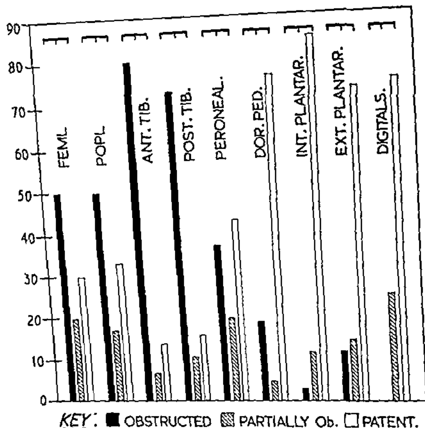


FIG. 199

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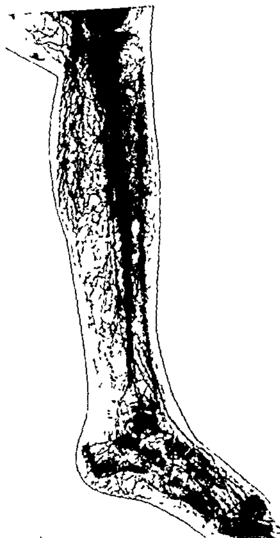


FIG 202
Same case as Figure 203 None of the main leg trunks are patent below the popliteal The arterial pattern in the foot is good



FIG. 200
Femoro-popliteal obliteration. Patency of all vessels in the lower leg: anastomosis through sciatic nerve arteries (Case W. 73)



FIG. 201
Pedal and digital vessels of Figure 200

the subcutaneous vessels certainly contributed largely to the maintenance of the circulation

Case W. 57 (Mr. F.)—Peroneal artery supplying leg and foot.—A man aged sixty-eight who had suffered from claudication for six years. He had not worked for five years. Two year ago trophic changes commenced which yielded for a time to conservative treatment. Amputation now performed for pain and trophic changes (Fig 204). The leg when received was cyanosed. Injection and dissection showed a narrowed popliteal trunk just below the level of the tibial head, and obliteration of both tibial arteries at their origins and throughout their lengths. The only large vessel patent is the peroneal (Fig. 205) which by its terminal anterior branch supplies the dorsalis pedis and by its posterior the plantar vessels, thus completing the plantar arcade.

This last pattern of vascularity (the "peroneal leg") is the single one which recurs with any frequency. In our series there has been an incidence of 38 per cent of peroneal legs. It is of interest to know whether, when both legs become the seat of severe occlusive disease, there is any symmetry in the vascular patterns. I have examined and dissected six such cases and find the lesion remarkably symmetrical in four of them, the main patent artery being the peroneal in two pairs of legs, the posterior tibial in one, and the anterior tibial in one. The figure (Fig. 206) shows tracings of the arteriograms in the last-mentioned case.

Thrombosis.—The progressive nature of atherosclerotic ischaemia is liable to exacerbations due to the occurrence of thrombosis. This may not at the time necessarily give rise to clinical manifestations which are recorded either by the patient or by the surgeon. In a certain number of cases, however, the thrombosis of an important and previously narrowed trunk, such as the femoral or popliteal, may be an event which precipitates gangrene in a limb already the seat of silent ischaemia. We have found recent thrombi in 57 per cent of our cases in one or other of the main arteries. The thrombi frequently show signs of canalisation which seems to proceed quite actively in spite of advanced disease in the vessel wall Apart from these major thrombi there are also minor and recurrent arterial thromboses which play a part in the silent progress of the disease; a part which is difficult to evaluate but is no doubt considerable. On histological grounds, it is not always easy, and may be impossible, to decide at a late stage how much of an old obliterative arterial lesion is due to thrombosis and how much to atheroma pure and simple. The case for mural thrombosis as a cause of atheromatous patches has been lucidly urged by Duguid, but there are difficulties in extending this explanation very widely, not the least being *the totally different* picture found in so purely a thrombotic process as Buerger's disease. The picture of a terminal thrombotic process causing the final occlusion of a lumen greatly narrowed by atheroma is

Case W. 73 (Mr. M.)—Femoro-popliteal obliteration.—The symptoms were of extreme claudication, pain and erythralgia with absence of all pulses in the leg. The limb was cold with the foot red and trophic ulceration present in the great toe. Amputation was performed at mid thigh. At the amputation site there was complete obliteration of the femoral trunk of old standing, and this extended as far as an inch below the head of the tibia. Injection at the amputation site being impossible this was effected through the posterior tibial artery at the ankle. The result showed good patency of all the three leg vessels below the obliterated popliteal. The main supply of the leg was through the *arteria comitans nervi ischiadici.* The dorsalis pedis artery was obstructed by atherosclerotic endarteritis, but the plantar and digital vessels were well filled through the posterior tibial artery (Figs. 200 and 201).



FIG. 203
Gangrene in a female diabetic aged 69.
(Case W 55)

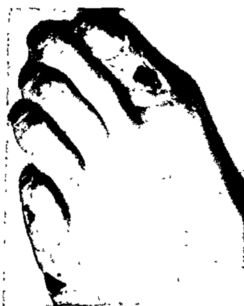


FIG. 204
Trophic changes from senile atherosclerosis
(See Fig 205)

Case W. 55 (Mr E.)—Patency of the popliteal artery with obliteration of all the main leg vessels.—This is at the opposite extreme from the last case. The patient was a female diabetic aged sixty-nine Amputation was performed through mid-thigh for gangrene of the great toe and severe pain (Fig 203) Injection of the popliteal artery showed that the vessel terminated at about the lower angle of the popliteal space and below this, although there was a rich vasculature, none of the main trunks was recognisable in the leg, until just above the instep where the dorsalis pedis artery showed (Fig 202). The general vasculature of the foot was remarkably intact. So great was the plexus of small anastomotic arteries in the leg that it was difficult to decide how the blood was distributed between them, but

a common one, and I think generally unmistakable (Fig. 207). Often such occluding thrombi are well organised by the time the limb reaches the stage of amputation and show some degree of recanalisation, but this can never be very effective, considering the small size of the new channels thus provided and the previous reduction in the vessel's calibre caused by atheroma.

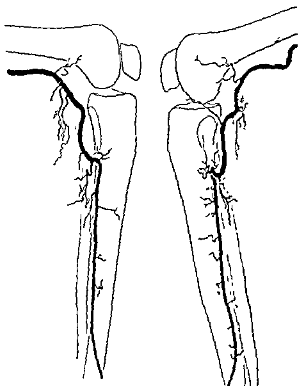


FIG. 206

Tracings of arteriograms in a woman aged 74 whose two legs were amputated at an interval of eleven months, showing symmetry of the lesions, the anterior tibial vessel alone remaining patent in each limb

We may quote the following case as an example of the influence of acute thrombosis:—

Case W. 103 (Mr. M.). Male age seventy-six.—A sufferer from diabetic atherosclerosis, for which right leg had been amputated previously. Cramp in the left leg and ulceration of the left big toe occurred and were treated conservatively for about two years, but for the four weeks prior to the amputation of this leg the pain became very severe and the ulcer increased in size. On examination the foot and toe were dark and dusky and there was an ulcer on the medial aspect of the great toe. Pulsation was present in the femoral artery, but none in the leg



FIG. 205
The peroneal artery supplying the whole leg and filling the foot vessels by its anterior and posterior branches (see also Fig. 204)

VENOUS THROMBOSIS —Venous thrombosis in atherosclerotic ischaemic disease and gangrene of the extremities is generally conspicuous by its absence Occasionally one finds recent red thrombi in localised stretches of veins, but very rarely is venous thrombosis extensive, either in regard to the length of vessel involved or to the number of vessels affected. It is not uncommon to find patches of organised venous thrombosis in ischaemic limbs: these do not seem of any importance in view of the numerous venous anastomoses nor, in fact, do we know how often they occur without associated ischaemia in elderly subjects, such as those who are typically affected by atherosclerosis. In this series substantial venous thrombosis of a degree likely to have affected the circulation was only present in 10 per cent of cases. The matter is quite otherwise in Buerger's disease, or in traumatic gangrene, in both of which venous thrombosis is often an important element

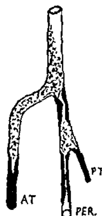


FIG 208 Recent thrombosis occluding arteries narrowed by atherosclerosis. (Case W. 103)

THE HISTOLOGY OF ATHEROSCLEROSIS

It cannot be too strongly emphasised that the changes in the arteries which occur in atherosclerosis, and which result in ischaemia, are extremely patchy By this it is not meant that stretches of disease in the vessel alternate with stretches in which the vessel is healthy, but rather that whilst a main leg artery may be diseased over its whole length, from its origin to where it splits up to form the foot vessels, with some degree of narrowing throughout, this latter is commonly focally intensified so as to produce complete occlusion. For this reason a few random sections taken across certain of the vessels give no idea of the extent or complexity of the arterial disease. The occluded stretches may be long or short, and alternate with stretches in which the full bore of the artery may be retained, or with others in which this is reduced to a mere pin-point At the risk of being repetitive we would point out that these eccentric and capricious narrowings must produce the most extreme changes in the flow of blood, which will be hurried through the narrows and stagnant in the widely patent portions of the arteries

The process which leads to the vascular narrowing is essentially a thickening of the intima, *i e.*, that portion of the wall which lies inside the internal elastic lamina. In the larger vessels
there
contai
(Fig.

In the three main leg arteries, however, which are smaller, the tendency is for there to be a more uniform, though generally also eccentric, layered fibrous hyperplasia, the new material being composed of a loose acellular and avascular and often oedematous fibrous tissue, which surrounds, diminishes,

arteries. Oscillometry above the knee was six, below the knee nil. Mid-thigh amputation was performed.

On injection a complete block from old atherosclerosis was found at the lower end of the popliteal artery just distal to the origin of the anterior tibial artery.

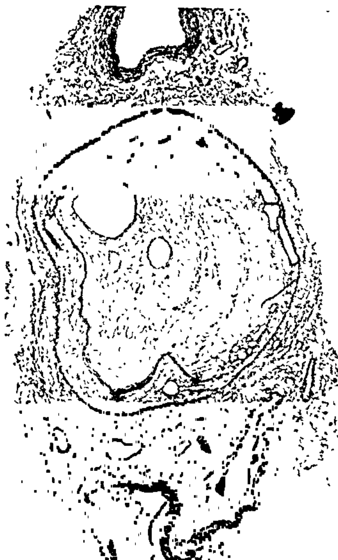


FIG. 207

A posterior tibial artery showing partial obliteration by an eccentric atheromatous plaque, the obliteration being completed by a thrombus which has become partially recanalised × 15

There was recent thrombosis of the popliteal vessel from a point a little above this and extending into the anterior tibial vessel. The latter was patent in the upper part of the leg, but occluded by old disease at mid-leg where the peroneal took over the chief supply. The condition which is illustrated in the diagram (Fig. 208) is one of old occlusive disease complicated by recent thrombosis.

of lipoid infiltration, necrosis, and at times calcification and ossification. In this it differs very much from the thrombotic occlusion seen in Buerger's disease

To avoid a wearisome account of the various phases and differences seen in the histological examination, we may illustrate the changes seen in the various vessels in a single typical case.

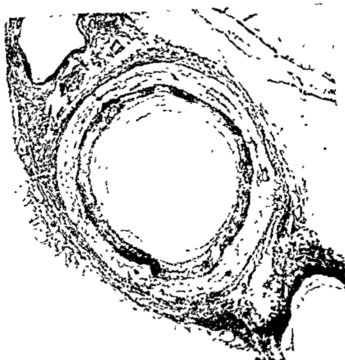


FIG. 210
Peroneal artery showing concentric atheromatous narrowing × 30

Case W. 36.—A man, aged seventy-five, who was admitted to hospital on account of grangrene of the left big toe No pulses were felt in the leg. The toe was black and shrivelled, with a line of demarcation. A mid-thigh amputation was performed. The examination of the limb showed complete obliteration of the popliteal artery, beginning at a level about 2½" below the joint and extending over a distance of about 2". The posterior tibial artery then emerged as a flaccid and patent trunk which was the main artery of supply to the leg and foot The peroneal and anterior tibial arteries received a little anastomotic filling in the lower third of the leg only

The condition of the vessels is shown in Figure 211 and the corresponding histological changes at various levels in Figure 212. The lesions in the individual arteries are:—

and finally may occlude the lumen (Fig. 210). This central occluding tissue is often soft and gelatinous and appears to the naked eye, in the dead limb, as a greyish avascular plug when the occlusion is complete. This endarteritic overgrowth may either itself occlude the lumen or final occlusion may be brought about by thrombosis. It is often difficult to say at a late stage which of these



FIG. 209
Eccentric atheromatous narrowing of the popliteal artery ×8

processes is responsible, or the extent to which they are combined. No one who studies the question in these peripheral arteries can fail to be impressed by the frequency with which thrombosis complicates atheroma; extending to the latter term the special fibrous intimal changes such as we have just described which occur in the peripheral arteries as the associate of typical atheromatous plaques in the larger and more central vessels.

Some writers, *e g.* Lindbøm, seem to think of arterial occlusion solely in terms of thrombosis and the increase of atheromatous patches by haemorrhage. We are not prepared to say to what extent thrombosis dominates the process of progressive occlusion, but believe that atheroma alone plays a very important part. The solution of the question is complicated by the difficulty in distinguishing atheroma from the late stages of thrombosis (Duguid). But whatever its distribution, and whatever part thrombosis plays, *this arterial disease constantly bears the hall-mark of a degenerative change*, in so much as the tissue which occludes the vessel is avascular and acellular and the seat

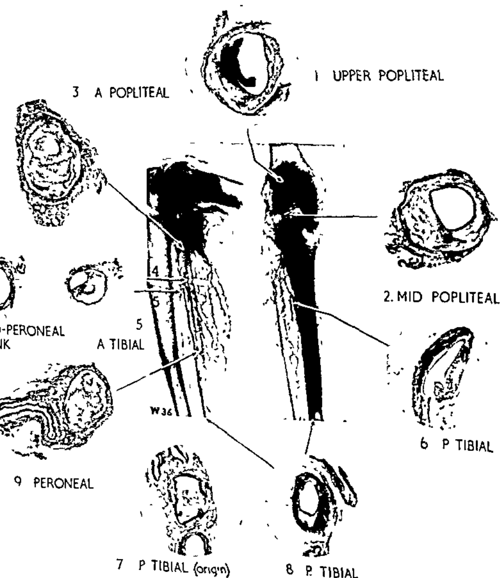


FIG 212
Histological detail of vessels in Case W 36 (Fig 211)

1. Upper popliteal.—In part calcified and very *atheromatous, with recent red mural thrombus in a vessel already* narrowed by an old occlusive lesion which is in part thrombotic.

2. *Mid-popliteal.*—Vessel calcified and lumen reduced to about one-third. The occlusion has the appearance of classical atheroma.



FIG 211

Obliteration of the lower part of the popliteal artery The supply to the leg is by a patent posterior tibial vessel (Case W. 36)

3. Lower popliteal.—Complete occlusion by an organised *thrombus*, complementing advanced atheroma.

4. Tibio-peroneal trunk.—Over a stretch of about 1″ this is widely patent with a little atheromatous narrowing and some medial calcification

5. Anterior tibial.—Extremely narrowed at its origin by a large atheromatous plaque which is both calcified and ossified, the lumen of the vessel being reduced to about one third.

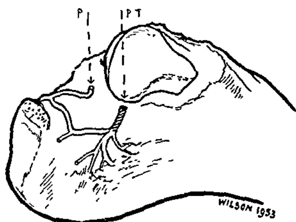


FIG. 214
Anastomotic supply by the peroneal artery to the plantar vessels in obstruction of the posterior tibial artery: a common arrangement.

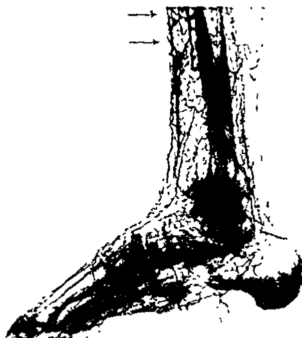


FIG. 215
Obstruction of the anterior tibial artery. Anastomotic vessels pass out between the muscles of the anterior compartment and run down subcutaneously to fill the dorsalis pedis. (Case of thromboangiitis, W. 121.)

6. Posterior tibial.—Below its origin is flaccid, collapsed and empty, with a single atheromatous patch.

7. Posterior tibial.—Occluded at its origin.

8. Posterior tibial 4″ above the ankle.—Patent with slight atheromatous narrowing.

9. The peroneal artery, below its origin.—Completely occluded.

The case then is one of extensive disease, with occlusion of the three main leg arteries below the popliteal space with typical histological changes, and a patent posterior tibial vessel filled by anastomotic channels.



FIG. 213
Arterial arcades of the leg and foot (M A and P A are the metatarsal and plantar arches) with the dorsal and plantar interosseous arteries and their communicating vessels

THE ADAPTATION OF THE CIRCULATION TO ARTERIAL OCCLUSION IN ATHEROSCLEROSIS

This involves two problems—

(*a*) The establishment of a collateral circulation, as usually understood, and

(*b*) The canalisation of thrombi.

Collateral circulation.—This is due to the enlargement of pre-existing, and often named, arteries. These are usually parts of some minor arterial arcade which enlarge to accommodate the blood. The exact vessels involved depend upon the site and extent of the lesions in the larger arteries.

We have already (p. 340 and Fig. 199) referred to the frequency with which the peroneal artery escapes disease and we would here emphasise the importance of this vessel for the circulation of the foot. This is obvious when we consider its anatomical connections and the contribution it makes to the peripheral arterial arcades (Fig. 213) The anterior and posterior terminal branches of this vessel anastomose with the dorsalis pedis and posterior tibial arteries low down in their course, and often below the level at which they are obstructed Secondary arcades, uniting these two systems, are provided by the plantar, tarsal and metatarsal arches, whilst the plantar and dorsal interosseous vessels, springing respectively from the plantar and metatarsal arches are united by perforating branches. The foot thus possesses a whole series of arterial arcades which may be supplied from one or both ends by the terminals of the peroneal artery

In a case in point (Case W. 57 p. 345 and Fig 205) the anterior and posterior tibial arteries were obstructed and the ingress of blood to the foot, which had a good vasculature, was mainly through the peroneal. Dissection showed

out from above the level of obstruction between the tibialis anticus and extensor longus digitorum muscles which, passing down subcutaneously, connects with the dorsalis pedis beyond the anterior annular ligament (Fig. 215).

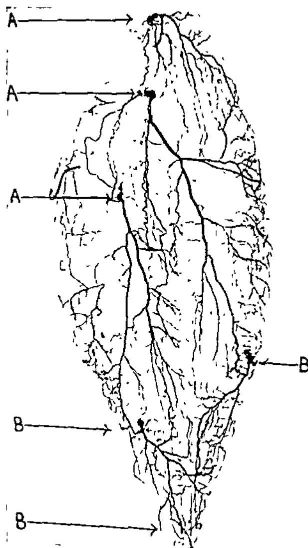


FIG 217

The superficial ...

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the supply to this was by a posterior terminal branch of the peroneal which passed beneath the tendo Achilles and opened into a short segment of the distal posterior tibial, which was patent just at the point of its division into the two plantar vessels (Fig. 214).

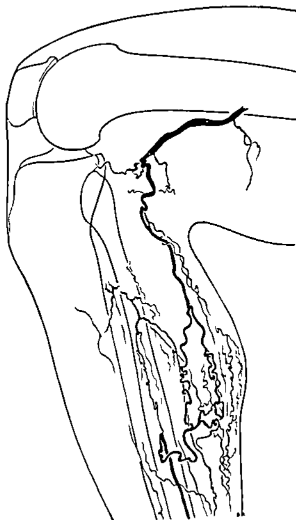


FIG. 216

... astomoses of

Other collateral vessels are especially those in the areolar tissue of the intermuscular planes, the arteriae nervorum, and the arteries in the subcutaneous tissue Arteries within the muscular fascial compartments of a limb do not penetrate these to any very great extent. When a subcutaneous anastomosis develops, to short-circuit an occluded stretch of a large vessel, the connection is made by vessels passing in the loose tissue between these compartments. For example, in obstruction of the lower end of the anterior tibial artery a subcutaneous connection may often be found by a vessel passing

out from above the level of obstruction between the tibialis anticus and extensor longus digitorum muscles which, passing down subcutaneously, connects with the dorsalis pedis beyond the anterior annular ligament (Fig. 215).

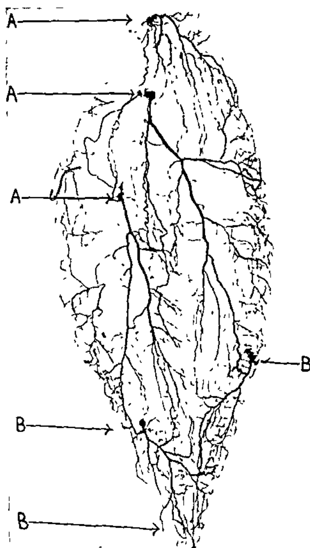


FIG 217
The superficial anastomoses of the upper (A) and lower (B) groups of arteries to the soleus muscle, permitting a communication between the posterior tibial and peroneal arteries

The arteries which accompany the ner[illegible]

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the supply to this was by a posterior terminal branch of the peroneal which passed beneath the tendo Achilles and opened into a short segment of the distal posterior tibial, which was patent just at the point of its division into the two plantar vessels (Fig. 214).

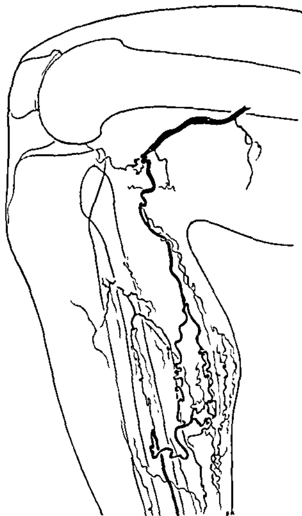


FIG. 216
Tracing of arteriogram showing anastomoses of popliteal and posterior tibial vessels by way of the superficial anastomoses of the arteries to the gastrocnemius muscle

Other collateral vessels are especially those in the areolar tissue of the intermuscular planes, the arteriae nervorum, and the arteries in the subcutaneous tissue Arteries within the muscular fascial compartments of a limb do not penetrate these to any very great extent. When a subcutaneous anastomosis develops, to short-circuit an occluded stretch of a large vessel, the connection is made by vessels passing in the loose tissue between these compartments. For example, in obstruction of the lower end of the anterior tibial artery a subcutaneous connection may often be found by a vessel passing

muscles, such as the gastrocnemius (Fig 216) and will here provide a connection between the popliteal and posterior tibial arteries; or in the soleus (Fig. 217) permitting a connection between posterior tibial and peroneal arteries. It seems only reasonable that where a suitable pressure gradient exists—and the anatomical changes found in the vessels give ample evidence of such a possibility—that these vessels may act as important collateral channels. Barcroft[12] and Dornhorst have produced experimental evidence for the existence of a by-pass mechanism in muscles and though they postulate an arterio-venous connection it is possible that the facts just mentioned may contribute to their results. Finally, we may say that the enlarged vessels which carry the collateral supply are generally found to be relatively thin-walled and with a disproportionately large lumen (Fig 218—*see also* Fig. 253). The lack of hypertrophy in thickness of the muscle fibres may be due to the fact that the blood they transmit is at a relatively low pressure, but the precise nature of the stimulus which produces this special form of simple enlargement of lumen is unknown Clearly its effect is more favourable, from the point of view of the quantity of blood passed through the vessel, than would be an increase of the muscle fibres in all dimensions. In concluding this story of the collateral circulation we may point out that there is no evidence of neo-genesis of arteries.

Associated venous changes.—The venous system is so capacious and variable, and has such abundant connections, that it is hardly to be expected that it will react in any noticeable way to local arterial ischaemia. Nevertheless we have been struck repeatedly with the apparent diminution in size of the veins which accompany arteries which have been occluded over long stretches; so much so that we think that arterial occlusion in such cases is often a real cause of venous atrophy. The matter is one which awaits further investigation.

Canalisation.—When we come to consider the way in which the circulation is restored in the individual vessel—as distinct from the provision of an alternative route for the blood—we face an entirely different problem. We have to deal with an occluding thrombus and the problem for the tissues is to provide a way for the blood through the clot A thrombus may be subject either to organisation by the classical process, involving its invasion by *vasa vasorum*—much as a pericardial exudate is organised by the pericardial vessels—or it may be canalised by a wholly different mechanism. The first process

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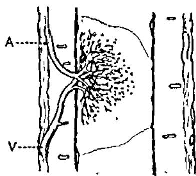


Fig 219
Diagram of the organisation of a thrombus by the *vasa*

small arteries in the popliteal space, was derived *from the A. comites n*
ischadici).

In addition to these connecting arteries the plexuses of peri-arte
vessels may also provide a by-pass in obstruction, not only circumventing t
but permitting blood to pass from one arterial trunk to another.

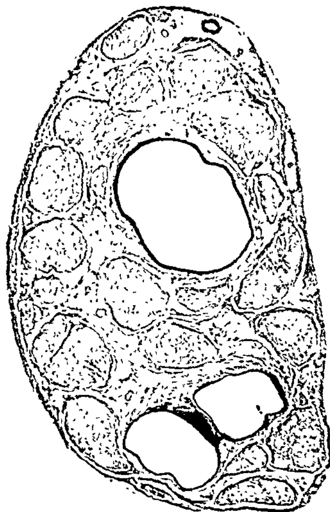


FIG 218
Enlargement of the arteries of the sciatic nerve in obliteration of the femoro-popliteal trunk Note the large lumen and thin walls × 18

The part played by the vessels of the muscles is generally considered tc
be minimal. My own observations have shown me that under certain condi-
tions, where a length of an artery is obstructed, peripherally injected material
finds its most easy passage from the patent distal to the patent proximal part
of an artery through the large intramuscular arterial anastomoses without
opening the capillary bed. These anastomoses are very considerable in certain

Roux's third stage of vascular development.* In some vessels only tenuous bands and ill-formed vessels remain in the lumen, in others there is a development of well-formed arterial or venous trunks with the muscle and elastic tissue appropriate to their structure. It may be mentioned, in supporting the view that there is a specific stimulus directing the formation of these vessels, that in arteries the structure of mature new-formed vessels is arterial, and in veins



FIG. 221
Area C, Figure 220. On the right are fibrinous strands containing masses of cells. On the left side these are disappearing, leaving open lacunae. ×130

venous. The process of lacunar canalisation may, be it understood, be associated with a certain amount of organisation from the irruption of *vasa vasorum* through the vessel's wall—though in my view the two processes are fundamentally distinct—and there may develop accordingly two circulations in a canalised vessel: one, the *through circulation*, and the other a local arterio-

* Roux defined the stages of vascular development in the foetus as —
1. The stage of *genetic factors*. Here capillary development begins, and proceeds for a limited time without the presence of a circulation, as in the capillaries of the yolk sac.
2. A stage of *adaption* in which the circulation is established and the primitive axial system of the limb becomes adapted to the special features of the species, by the development or suppression of vessels.
3. A stage of *haemodynamic factors*, in which the full development of the vascular system is associated with haemodynamic influences which are supposed to be a directing cause, though this is far from proven.

and venules. Such blood as enters and leaves is primarily supplied by pre-existing small vessels coming from, and returning to, the adventitial network This result contributes little or nothing to the re-establishment of the occluded circulation. The effect is shown in diagrammatic form in Figure 219. The re-canalisation of the thrombus so as to provide a *through* flow of arterial or venous blood (in artery or vein) is by what I have called "*lacunar*" *canalisation.*[13] The lines of this process are laid down from quite early stages in a thrombus, in which the denser strands of fibrin become covered by endothelial cells which have the capacity to multiply with remarkable rapidity. Next, the looser parts of the clot, between such endothelialised strands, are removed by

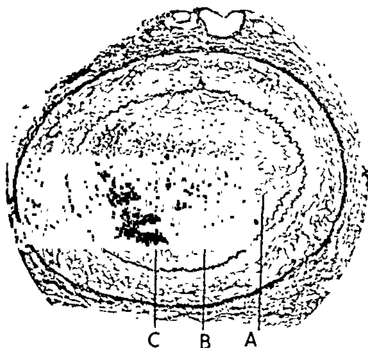


FIG. 220
Thrombosed popliteal artery undergoing canalisation
(Case W 30) ×20

phagocytic action or autolysis leaving a sponge-work in which blood quickly begins to circulate. A further stage is the laying down of reticulin fibres in the substance of the endothelialised bands, and their slower conversion into collagen bands. Many of the larger lacunae, often the largest, develop between the occluding thrombus and the vessel wall, where it may be expected that endothelial overgrowth is most abundant.

The later development of this canalised cavernous tissue is dependent upon factors which are unknown, but may be similar to those operative in

venous circulation, which nourishes new-formed tissue but has little or nothing to do with the main flow of blood.

The accompanying figures illustrate the above points. A thrombosed artery is photographed (Fig 220) from which the three marked areas C, B and A are shown at higher powers. The various stages may be followed from left to right. Area C (Fig. 221) shows the fibrin bands of "unorganised" thrombus, in the interstices of which are numerous leucocytes In area B (Fig. 222) these leucocytes are shown to be disappearing, leaving lacunae

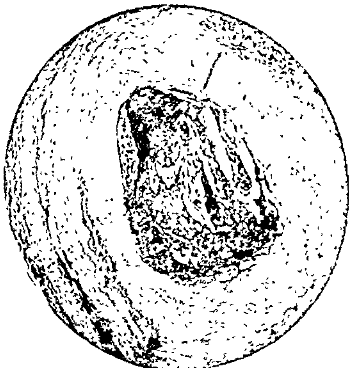


FIG 224
Lacunar canalisation of a thrombus in the popliteal artery of a man of 72. ×20

bordered by the fibrinous bands which are partially endothelialised and in process of conversion into collagenous bands. In area A (Fig. 223) the process has advanced further, the lacunae being converted into round dilated vessels. Such a later stage is also illustrated in Figure 224 where a thrombosed vessel is shown filled with such lacunae which at this stage, although developing fibrous walls, show no further differentiation, but Figure 207 shows a familiar late picture of recanalisation, and the merging of many channels into a single main channel with a number of lesser channels which have acquired a definite vascular form. It is not uncommon for the larger new-formed vessels in a



FIG. 222
Area B, Figure 220 Endothelialisation and partial fibrous transformation of lacunar walls × 130.



FIG. 223
Area A, Figure 220. Showing, from right to left, the transformation of irregular lacunae into rounded vascular channels × 130

CHAPTER IX

THE SURGERY OF ATHEROSCLEROSIS

THE use of the term "arteriosclerosis" rather loosely for any degenerative condition of arteries has led to some confusion. There are three conditions particularly which tend to be included under this heading—Monckeberg's sclerosis, arteriolosclerosis and atherosclerosis

Mönckeberg's sclerosis[1] is a disease of the media of arteries, involving vessels of all sizes from the largest down to those the size of the digital arteries, characterised by calcification of the diseased media, and not giving rise to obstruction of the affected vessels. The well known pipe-stem arteries are examples of this condition. The arteries continue to function as conduits, and there are no ischaemic symptoms resulting from the disease.

Arteriolosclerosis is a disease of arterioles occurring in the association with hypertension and renal disease, and it may or may not be associated with other varieties of arterial degeneration

Atherosclerosis is a degenerative disease of the larger arteries; it probably never affects vessels the size of the digital arteries. The disease consists of subintimal deposits of lipoid material which may become the site of calcification or which may ulcerate with resultant secondary obstruction from thrombosis giving rise to symptoms attributable to ischaemia. In any one patient there may be atherosclerosis, Monckeberg's sclerosis and arteriolosclerosis but more frequently the conditions exist separately.

It is with atherosclerosis that we are concerned in this section.

Atherosclerosis is known to have existed from ancient times. Ruffer[2] found typical lesions in Egyptian mummies 3,000 years old and the association of hardening of the arteries with gangrene has been recognised for three centuries, but it was not until the middle of the eighteenth century that atherosclerosis was described by Crell[3], the first detailed description being given by Morgagni.[4] In 1904 Marchand suggested the name atherosclerosis instead of arteriosclerosis In the last fifty years a vast amount of literature has appeared on the subject but although there have been great advances in the treatment of the symptoms of the disease nothing has been achieved, though much has been suggested, as regards the cause or the prevention of the disease process. An historical review of arteriosclerosis has been made [illegible][5] The importance of [illegible] [illegible]out six times as many [illegible] many are hopelessy c[illegible] [illegible], coronary and peripheral arterial disease.

recanalised artery to become highly organised, developing a muscular coat and occasionally an internal elastic lamina.

Onset of Gangrene

The actual condition of gangrene may arise (1) either by the slow progress of the arterial occlusion until it reaches a stage at which the oxygen supply is reduced beyond the minimum required for the life of the tissues, or (2) from an increased demand of the tissues due to injury or infection in the ischaemic areas, or (3) from superadded vascular occlusion. The latter may either be arterial embolism or thrombosis, or venous thrombosis. In our experience in the examination of pathological material we think that acute thrombosis of a distal artery—such as a digital artery—is a common late occurrence In any case it is quite usual to find a recent thrombus, with acute vascular changes, in one or other of the arteries immediately supplying the necrotic tissue. It is, of course, open to question whether the artery becomes thrombosed and the tissue dies in consequence, or whether the arterial death is merely part of the ischaemic death of a larger area—as put forward in (*1*), above. The appearances however do suggest that there is commonly a *terminal* acute arterial thrombosis in one of the smaller vessels going to the gangrenous area. Such a vessel shows inflammatory changes in its muscular coat, a recent fibrinous thrombus, and peri-arterial inflammatory changes which merge with those at the border of the gangrenous zone. The presence of a fibrin thrombus points to the occlusion having taken place whilst there was still an active circulation in the affected vessel and suggests that this thrombosis, due no doubt to alterations in the vessel wall from increasing anoxia, was the precipitating factor in the gangrene. In general, venous thrombosis seems a less important, and even later, event. We have not seen unmistakable pathological evidence of distal arterial obstruction by embolus, such as might arise from the detachment of a portion of thrombus from an atheromatous area, in cases of this sort. If it occurs it would in any case be difficult to find and identify with certainty.

J. H D.

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In a post-mortem study it was found that patients who had suffered from diabetes for twenty years or more rarely escaped some *degree of atherosclerosis*, but that those who had suffered for ten years or less had little tendency to develop this condition[12] Vascular complications appear to occur in relation more to the duration of the diabetes than to its severity and clinically there is no increased incidence in patients with diabetes of less than five years' duration, but there is a very high incidence in patients who have suffered for more than fifteen years.[10] On the other hand Root *et al*[13] consider that the severity of the diabetes has an important influence on the development of atherosclerosis, and have shown that very careful control of the diabetes will delay or even prevent its onset

In spite of the evidence that long standing diabetes leads to atherosclerosis, the average age of patients who suffer amputation for atherosclerotic gangrene seems to be the same in diabetics and in non-diabetics. At Hammersmith Hospital the average age for amputation in atherosclerosis uncomplicated by diabetes is seventy-three, and complicated by diabetes seventy-one, and in another hospital the corresponding figures are seventy-one and seventy-two. These facts suggest that the arterial degeneration in diabetes which is often assessed by ophthalmoscopic findings and by the presence of calcification of the vessels shown on X-ray may be slow to cause anoxia of the extremities

Although diabetes is more common in women, atherosclerotic gangrene occurs more commonly in diabetic men. These facts seem to show that diabetes does not predispose to a type of arterial obstruction giving rise to ischaemic symptoms in the limbs

Lundbaek[14] considers that diabetes may give rise to specific vascular changes affecting principally the most distal vessels, and he has called this condition " diabetic angiopathy " and in a considerable number of cases of gangrene occurring in diabetics, the popliteal pulse, and even the pulses at the ankle joint are palpable, an almost unknown finding in gangrene complicating atherosclerosis.

In the diabetic patient with neuropathy, many symptoms occur which resemble those resulting from atherosclerosis. Pain, coldness, numbness and cramps, and even gangrene are frequent, all in the absence of arterial obstruction Gangrene is frequently initiated by an injury or burn or by sepsis that has not been noticed by the patient, and occurs in extremities with adequate and unembarrassed blood supplies, and it is of a traumatic or *infective type.* These symptoms may mimic those of an arterial obstruction which is not in fact present

SYMPTOMS

Atherosclerosis is frequently extensive and has often been present for many years before symptoms appear. Routine post-mortem examinations show that obliteration of arteries may be present without evidence of the disease during life. It is only when the degree of arterial narrowing or

INCIDENCE

Age.—Atherosclerosis is predominantly a disease associated with ageing, and is often accompanied by arterial obstruction. It has been reported that some degree of intermittent claudication is present in 1·1 per cent. of all persons above the age of seventy years.[6] At the other end of the age scale coronary arterial occlusion from atherosclerosis has been seen in children in the teen-age group, and one fatal case with calcification of the coronary arteries has been reported in a child of three years.[7] Although coronary atherosclerosis with obstruction is not uncommon in the third decade, disease of the limb vessels with symptoms from obstruction is unusual before the age of forty years, after which it becomes increasingly common. Hardened and calcified arteries without obstruction are found frequently during routine examination for some unrelated condition before the age of forty years.

Sex.—Atherosclerosis accompanied by evidence of ischaemia occurs in men seven times as often as in women, although the incidence of atherosclerosis without arterial obstruction is only about twice as common in men[8] It seems that there is a greater tendency for thrombosis to occur in men with atherosclerosis than there is in women It may be that the heavier physical work undertaken by the male sex is a factor, but against this concept is the fact that coronary artery obstruction is relatively more common in doctors than it is in miners, and, therefore, hard physical work does not seen important in the aetiology.

Hypertension does not appear in our experience to be a particularly [illegible] common in [illegible] of this.

Race.—There does not seem to be conclusive evidence that atherosclerosis is more or less common in any particular race, which would seem to indicate that dietary factors are unimportant. Ruffer found arterial lesions in Egyptian mummies 3,000 years old and also in Mohammedan pilgrims, occurring with an incidence similar to that seen in Europeans, and Egyptians cannot be considered excessive meat eaters. It has been suggested, but there is no proof. that the disease is less common in Chinese, who are largely vegetable eaters. If a diet low in protein was a factor in the prevention of atherosclerosis, it would be thought that the incidence of the disease would be high in Eskimos whose diet is largely meat, but this has not been found to be so. On the other hand many consider a high fat and protein diet to be a significant factor in the genesis of the disease.[9]

Climate has no influence on the incidence of the disease.

Diabetes.—Greatly differing estimates have been made of the incidence of arterial disease in diabetes, and figures varying from 92 per cent.[10] to 3 per cent.[11] are recorded by different authors.

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obliteration is such that there is insufficient blood available for the tissues to function properly that symptoms occur. The early symptoms depend on the structures which first suffer as a result of diminished blood supply, and since in atherosclerosis it is the larger vessels which are primarily affected, the *burden of ischaemia falls on muscles rather than* on the skin and subcutaneous tissues. Consequently intermittent claudication is the commonest presenting symptom, though rarely trophic changes, persistent sepsis, ulceration or even gangrene may first occur, especially in those patients whose activity is so limited by custom or intercurrent disease that claudication is never a complaint

The calf muscles are generally the first to originate the pain. In the early stages, symptoms from ischaemia may amount to little more than excessive fatigue after exercise, but as the ischaemia increases in severity, pain takes the place of fatigue and may vary in degree from a slight ache occurring after walking half-a-mile or more to a severe intolerable cramp occurring after a few yards. Intermittent claudication is not limited to the calf, but may occur in the feet when it is often described as a feeling of walking on pebbles, presumably because of the numerous muscles in the sole of the foot. In atherosclerosis it is less common at this site as a presenting symptom than is the case in thromboangiitis obliterans This is because extensive obliteration of the vessels of the leg below the knee without involvement of the femoral or popliteal arteries is uncommon in atherosclerosis whereas in thromboangiitis obliterans it is more frequent, and the muscles of the feet suffer before those of the calf. In the later stages of atherosclerosis claudication in the foot occurs not infrequently when in addition to obstruction of the femoropopliteal trunk there is also obstruction in the tibial vessels, when *it may occur during exercise before the onset of pain in the* calf. Narrowing or obstruction of the aorta and iliac vessels may give rise to claudication of the gluteal and thigh muscles, often more of an ache than a severe pain, but there is usually claudication *in the calf muscles as well, even in the presence* of a patent femoropopliteal trunk

The gastrocnemius muscle is often supplied by an end artery from the popliteal, and occlusion of this may lead to ischaemic fibrosis, with the result that even though claudication does not occur, fibrous infiltration and contracture may; a similar phenomenon may occur in the biceps in the arm [15] Claudication pain may occasionally pass away as the disease progresses in which case there is marked wasting and weakness of the involved muscles, and the relief of pain is due to ischaemic atrophy of muscle with incapacity for contraction Claudication is unusual in the muscles of the arm and hand in atherosclerosis owing to the rarity of arterial obstruction in the upper limb, *but when it does occur it is manifest often by inability* to write more than a few words. We have seen an old lady with obstruction of the subclavian artery from atherosclerosis who was unable to knit more than twenty stitches before the *onset of pain.*

Intermittent claudication is sudden in onset, and severe at the outset when thrombosis suddenly obliterates a vessel the site of intimal disease, but after a few weeks pain may become less severe as the collateral vessels enlarge. Similarly it is gradual in onset when the obliteration of the vessel is slow and it may be present before obstruction is complete and occasionally in the presence of palpable though diminished peripheral pulses.

Muscle tenderness.—Lewis[16] has said that a muscle which claudicates is tender for an hour or so after recovery from the pain of claudication, and this assists in the detection of the particular muscle originating the pain.

Coarse fibrillation of muscle, well seen in the adductor hallucis, frequently results from long standing ischaemia.

Muscular weakness.—This occurs largely as a result of disuse, but sometimes from atrophy. In aortic or iliac obstruction wasting of the calf muscles is a common early sign.

Muscular paralysis, like sensory paralysis, is indicative of recent acute arterial obstruction and is almost always followed by gangrene unless recovery begins within a few hours of the onset of the paralysis.

Changes in the skin.—The colour of the skin, as Lewis[16] has described, depends on the circulation in the capillaries, and the temperature of the skin depends on the circulation through the arterioles. Warm pale skin indicates rapid flow through arterioles with a healthy skin not demanding any excess of blood, the capillaries therefore not being dilated and comparatively few of them being filled. Warm deeply coloured red skin occurs where skin has been irritated from any cause, *e.g.* by heat or inflammation with consequent high capillary flow. Warm deeply coloured cyanosed skin is present when there is defective blood supply of the skin resulting in anoxic paralysis of the capillaries and when such a part has been artificially heated as in a warm bed; cold cyanosed skin indicates slow or absent blood flow. Cold deeply coloured red skin occurs when the temperature of the part is 15°C. or less when oxyhaemoglobin does not dissociate, and when at the same time the capillaries are damaged and dilate, although the total flow through the part is small.

The return or rate of return of colour to skin following blanching induced by local pressure is a fallacious test of circulation, and depends on a sponge-like action, the blood being expressed from one area to another and returning from the surrounding area on release of pressure, without necessarily any advance along the vascular pathway.

Colour changes on elevation and dependancy are common, and the angle which the limb has to be raised from the couch before pallor appears is termed the "critical angle" and has been used as an index of the severity of the vascular occlusion. Return of colour to a foot following pallor induced by elevation is a sign of value and significance, and occurs in the normal in

a few seconds, and a delay of fifteen seconds indicate a moderate, and of thirty seconds a severe degree of ischaemia. Pallor is frequently seen in an extremity on activity, and is due to a shunt of the blood to the contracting muscle at the expense of the vessels of the skin. It is common in obstruction of the iliac arteries and the aorta.

Redness of the toes or feet on dependancy is frequent but it may be a minute or more before it appears after the limb has become dependent. It is due to ischaemic paralysis of capillaries, and is therefore a sign of rather severe ischaemia. Very different is the redness of toes or forefoot, or part of the forefoot, which is seen in most distal vessel involvement; it does not disappear or only incompletely disappears on elevation of the limb (p 331). This is due to almost complete stasis in the distal vessels and is evidence of venous as well as arterial thrombosis, and also the extravasation of red cells and products of the breakdown of haemoglobin in the tissue spaces. It is a change often associated with severe pain especially when the part is warm, and also with hyperaesthesia, and is more common in thromboangiitis obliterans than in atherosclerosis. A patchy cyanosis and pallor indicates a severe degree of ischaemia and a recent thrombosis.

Raynaud's phenomenon.—This is usually evidence of obstruction of the vessels of the digits but it also occurs, though uncommonly, where larger vessels are affected, and it sometimes involves the whole forefoot, when only the pallid phase and not the cyanotic phase is seen. It is uncommon in atherosclerosis.

Trophic changes in the skin.—Wasting and disappearance of the subcutaneous tissues of the digits together with loss of hair from the dorsa of the toes and smoothing of the corrugations give rise to a tapered, smooth and often shiny appearance, as if the skin were stretched tightly over the bones The nails are slow and irregular in their growth. Sepsis is common and arises as a paronychia or infected cut, scratch, blister, burn or from the application of some strong antiseptic, or as a result of injudicious chiropody. Such lesions are slow to heal and often result in ulceration and may rarely progress to a cellulitis of the foot and leg advancing with truly remarkable rapidity. A rather chronic low grade infection may sometimes involve the whole dorsum of the foot with superficial ulceration and sometimes later deep black gangrenous sloughs A paronychia with slow subungual extension is common, and frequently proceeds to gangrene of a distal phalanx or even the whole digit as a result of superadded thrombosis of nearby vessels. Gangrenous ulcers of the toes and feet and the region of the ankle often occur and may be limited to the skin and subcutaneous tissues (Fig. 225). Superficial dead tissue forms a black hard leathery slough and when removed there may be revealed apparently healthy granulation tissue which sometimes heals when relieved of the constriction of the slough. Ulcers over the lower and outer surface of the leg frequently occur and are usually painful. They often

fail to heal, and the associated pain demands amputation for its relief (Fig. 226). Constitutional symptoms are uncommon in sepsis associated with arterial occlusion except in those patients who suffer a rapid cellulitis



FIG 225
Pressure on the remaining heel of a patient bed-ridden after amputation often initiates gangrene—always painless but very slow to heal, if it does so at all.



FIG 226
Painful atherosclerotic ulcer which failed to heal Amputation was necessary for relief of pain.

Coldness and numbness of the extremities.—A complaint of coldness in : foot is frequent and this symptom occurring in one limb is strongly ggestive of ischaemia in that limb A hot water bottle is a constant require- ent in such patients, and there is a tendency to sit " on top of the fire."

Coldness is often aggravated by exercise and usually accompanied by a feeling of numbness when there is associated pallor. Numbness and pallor on exercise are indications of a major vessel block and result from a shunt of blood from the skin to the contracting muscles. If numbness of sudden onset is associated with sensory loss it is indicative of a sudden arterial occlusion with serious ischaemia, and unless sensation returns within a few hours, results in gangrene. There is often a hyperaesthetic area immediately proximal to the area of sensory loss.

Rest pain.—Pain when the limb is at rest is of different types and occurs as the result of :—

1. SEPSIS, particularly subungual, spreading from a paronychia It is throbbing in nature, and is eased by relief of tension. It also occurs in areas adjacent to ulcers and gangrene and is due to increase of tension within the tissues.

2. SEVERE ISCHAEMIA.—Ischaemic pain is only present when blood flow is minimal and it varies in intensity with the degree of ischaemia. It is in fact a reliable measure of its severity.

It is often associated with persistent rubor or pallor of the foot or part of the foot affected but may occur in the absence of colour change. It does not occur when the part is gangrenous, but is felt in adjacent areas if these are grossly ischaemic; if they are comparatively healthy, as they are in proximal arterial disease when gangrene of a toe results from embolism or thrombosis after trauma, pain is absent. The pain is situated over the affected area, spreading up one or other side of the foot, or may involve the whole foot, and is in the nature of a severe persistent gnawing ache with which are associated severe spasms and sudden " shoots " up the limb, but it bears no relation to any specific nerve territory. Spasmodic shooting pains are suggestive of obstruction of the femoral artery or a more proximal vessel. At first pain occurs in bed at night, when the part is warm, and the patient soon learns that relief may be obtained by putting the limb outside the bed clothes, preferably with the foot dependent on a chair or stool beside the bed, a position often leading to oedema. Pain increases in severity as the ischaemia advances and is soon present during the daytime too, the patient spending most of the time grasping and rubbing the foot in an endeavour to obtain relief. Even opiates fail to relieve the pain in the later stages and amputation is eventually welcomed. In fact, the improvement in the physical and mental condition after amputation is often most gratifying. Minor degrees of pain are relieved by sympathectomy as a result of increase of blood flow to the affected part Ischaemic rest pain is more common in thromboangiitis obliterans than in atherosclerosis, because of the severity of the distal ischaemia in the former condition (Chap VII). The existence of a specific ischaemic neuritis is in question (p. 424).

Temperature changes.—Though the ischaemic limb is usually cooler than its fellow, this is not always the case.[17] The limb must be exposed to room

temperature for ten minutes at least to allow it to cool before it is examined, when difference between the two limbs is then highly significant.

Changes in the bones and joints.—Rarefaction from disuse or infection is sometimes seen, and infection of joints from overlying ulcers is frequent. Periarticular fibrosis leads to stiffness of the small joints of the foot.

Swelling of a limb.—Swelling of an ischaemic limb is unusual but may occur from superadded deep venous thrombosis, persistent sepsis, prolonged dependancy or intercurrent cardiac or renal disease. In the absence of general disease it is a sinister sign and generally leads to amputation at an early date

Arterial pulsation.—Examination of the arterial pulses is the most important single examination in the evaluation of the ischaemic limb. Absence or diminution of the dorsalis pedis pulse is not always evidence of ischaemia, as this vessel is congenitally absent in approximately 8 per cent. of persons, and its place often taken by a prolongation of the peroneal artery. Absence of the posterior tibial, popliteal or femoral pulses is always significant, though in the presence of swelling of a limb, palpation of all but the femoral artery may be difficult or impossible The character of the artery, its resistance and tortuosity may be significant and should be noted. Collateral vessels over either femoral condyle, especially the medial may be felt and are indicative of femoropopliteal obstruction as they are not felt in normal persons. The Pachon oscillometer is helpful in determining the site of obstruction of a main vessel but gives no indication of the adequacy of the collateral circulation, nor of the circulation distal to the obstruction

A bruit may be heard, and a thrill felt over and immediately distal to a short segment of a major vessel, narrowed by disease.

GANGRENE

The amount of blood required to maintain the life of uninjured tissues at rest is very small, provided the blood has a normal haemoglobin content. A septic digit in an individual with a healthy arterial tree demands a blood flow about twenty times that of a normal finger. A precarious blood supply is inadequate to meet the crises of sepsis and repair, and permanent injury or death of tissue follows infection and injury.

In atherosclerosis the flow through the skin of the digits is generally adequate to maintain nutrition and the digits may be preserved throughout the life of the patient Distal gangrene involving a digit, a foot in whole or in part and rarely a hand, or a major part of a limb may nevertheless result in the following circumstances.

1. After trauma, physical, chemical or thermal.
2 From sepsis, giving rise to tension within the tissues and subsequent thrombosis of adjacent vessels

Coldness is often aggravated by exercise and usually accompanied by a feeling of numbness when there is associated pallor. Numbness and pallor on exercise are indications of a major vessel block and result from a shunt of blood from the skin to the contracting muscles. If numbness of sudden onset is associated with sensory loss it is indicative of a sudden arterial occlusion with serious ischaemia, and unless sensation returns within a few hours, results in gangrene. There is often a hyperaesthetic area immediately proximal to the area of sensory loss.

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6. From deep venous thrombosis still further embarrassing the circulation causing increased stagnation or a superadded reflex arterial spasm (p. 658).

In more than half the patients with atherosclerotic gangrene, injury is the precipitating cause.

Gangrene usually develops in the terminal parts of the digits, often in a nailfold associated with sepsis or as an ulcer which fails to heal or after blistering from a burn A whole toe, or toe with the adjacent part of the foot, and sometimes the skin of the heel or dorsum of the foot may be affected.

Rarely the whole foot, and very rarely the leg from the lower third of the thigh downwards becomes gangrenous At first there is loss of sensation, with pallor or cyanosis or a blotchy appearance with pallor and cyanosis. Eventually the whole part may become shrunken and mummified, though sepsis may occur at any time with upward spread of gangrene to the living tissue. There is no pain in the gangrenous area, and the adjacent living tissues may or may not be painful Pain is present if there is sepsis infiltrating and leading to tension within the living tissue and if ischaemia is severe, but pain is absent when there is no sepsis, and when the blood supply of the adjacent part is sufficient for life The colour of the skin is significant, as it is in the ischaemic limb without gangrene, and pallor or rubor persisting in spite of changes in posture suggest a critical blood supply, one which will probably be insufficient to maintain life. If the arterial obstruction has been sudden there is often a hyperaesthetic area in the skin proximal to the line of demarcation, although this is more common as the result of sudden occlusion of an otherwise healthy vessel, as by an embolus.

After a few days a line of demarcation between living and dead tissue appears, and if no treatment is undertaken, separation of the dead tissue may occur from suppuration, a slow and tedious process. If this occurs the living tissues have a blood supply which is sufficient to ensure healing after a local amputation, as tissues capable of forming pus have a considerable blood supply

Atherosclerotic gangrene is almost always dry in type.

GANGRENE AND DIABETES

Gangrene may occur in a diabetic patient who suffers from atherosclerosis and then it differs in no way from that occurring in uncomplicated atherosclerosis On the other hand diabetic neuropathies may result in loss of sensation of such a degree that local trauma, burns and sepsis are not felt, and gangrene may occur from failure to notice injury. An ill-fitting shoe, or a burn may result in gangrene in the presence of a good blood supply, and unnoticed sepsis may spread to involve the foot, with truly remarkable rapidity In such cases gas-forming organisms are usually present and there is crepitus over the swollen discoloured foot. Toxaemia is often severe but, surprisingly, not always so Gangrene occurring in the presence of severe

3. From extension of the disease leading *to obliteration of established* collaterals either by further *thrombosis* or by constriction of their origins by atheroma (p. 329). Massive thrombosis may complicate sustained *hypotension from illness*, operation, shock or chronic heart failure, although other physico-chemical changes in the blood may be contributory (Fig. 227).



FIG. 227
Atherosclerotic gangrene Massive thrombosis was precipitated during an attack of heart failure



FIG 228
Apart from the fourth toe, the rest of the foot is relatively healthy The patient had obstruction of the femoro-popliteal junction There is no complaint of pain as the toe is dead, and the adjacent tissues are not seriously ischaemic

4. From emboli arising from proximal atheromatous plaques or thrombi, lodging in the digital vessels (Fig. 228).
5. When in the presence of severe anaemia, the oxygen carrying capacity of the blood is so reduced that the diminished blood flow is insufficient for the life of the tissues.

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neuropathy is painless. It has been frequently suggested that the tissues of a diabetic are less resistent to infection than are the tissues of a non-diabetic. This has recently been criticised by Oakley (1954)[18] on the basis of the following observations.

1. Septic lesions in diabetics often heal readily without control of the blood sugar level.
2. Uncontrolled diabetics may never suffer from septic lesions in spite of daily injections of insulin.
3. Septic lesions are far more common in the feet than in any other part of the body.
4. Septic lesions of the feet are more common in elderly and long-standing diabetics than in young patients, although the diabetic condition is usually more severe in the latter.

These last two observations suggest that neuropathy plays the important part in the incidence of sepsis and traumatic gangrene of the feet. The neuropathies complicating diabetes not only affect the sensory nerves, but also the sympathetic nerve fibres with the result that vasomotor control is absent and the circulation in the digits does not respond to bodily heating and cooling.[19] This might appear to indicate a severe degree of arterial obstruction, an interpretation which can be avoided by observing the effect of an intravenous injection of 50 mg. of priscol on the skin temperature of the toes which rises owing to vasodilatation from the direct action of the drug on the vessel wall Such a loss of vascular control from nerve degeneration indicates that little benefit from sympathectomy can be expected in patients with marked neuropathies.

It is very important to distinguish those instances of digital gangrene. occurring in a diabetic patient, which result from neuropathy rather than from ischaemia The detection of pulses at the ankle joint, loss or diminution of sensation in the tissue proximal to the gangrenous area, and absence of pain all indicate gangrene of neuropathic origin. Severe ischaemia, pain, no loss nor diminution of sensation and typical colour changes involving adjacent living tissue, suggest a purely ischaemic cause, in fact an atherosclerotic gangrene. In those patients with moderate atherosclerosis, together with diabetic neuropathy, the parts played by each factor are difficult to estimate, but impairment of sensation and lack of pain suggest an important neuropathic element The presence of a palpable popliteal pulse suggests a predominantly neuropathic factor, for gangrene is rare in the atherosclerotic when the popliteal artery is patent A burn from a hot-water bottle or from sitting in front of a fire with the shoes off is more suggestive of neuropathic gangrene, particularly if it is of rapid onset, as even great heat may not be felt (Fig. 229). A line of demarcation forms more rapidly in neuropathic than in ischaemic gangrene, as the blood supply is more liberal, and the living tissue is more intolerant of the dead tissue. In doubtful cases it is wise to wait and see before a major amputation is undertaken, as limbs with



FIG. 229
A gangrenous ulcer from a hot water bottle burn in a diabetic Excision of the fifth metatarsal was necessary to allow approximation of the skin after excision of the ulcers. Healing followed.



FIG. 230
Diabetic gangrene in the great toe of a man aged 38 The toe was amputated after arteriography had shown good vessels adjacent to the gangrenous part. Healing occurred by second intention

neuropathy is painless. It has been frequently suggested that the tissues of a diabetic are less resistent to infection than are the tissues of a non-diabetic. This has recently been criticised by Oakley (1954)[18] on the basis of the following observations.

1. Septic lesions in diabetics often heal readily without control of the blood sugar level.
2. Uncontrolled diabetics may never suffer from septic lesions in spite of daily injections of insulin.
3. Septic lesions are far more common in the feet than in any other part of the body.
4. Septic lesions of the feet are more common in elderly and long-standing diabetics than in young patients, although the diabetic condition is usually more severe in the latter.

These last two observations suggest that neuropathy plays the important part in the incidence of sepsis and traumatic gangrene of the feet. The neuropathies complicating diabetes not only affect the sensory nerves, but also the sympathetic nerve fibres with the result that vasomotor control is absent and the circulation in the digits does not respond to bodily heating and cooling[19] This might appear to indicate a severe degree of arterial obstruction, an interpretation which can be avoided by observing the effect of an intravenous injection of 50 mg. of priscol on the skin temperature of the toes which rises owing to vasodilatation from the direct action of the drug on the vessel wall Such a loss of vascular control from nerve degeneration indicates that little benefit from sympathectomy can be expected in patients with marked neuropathies.

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FIG. 232
patient whose X-rays are shown in Figure 231



FIG. 233
The same patient after amputation of affected digits. Note the incisions extending on to the soles, to allow drainage After secondary suture the wounds healed (Fig 234)



FIG 234

neuropathic gangrene will heal with conservative treatment. Arteriography can be of great assistance, a good blood supply up to the gangrenous part suggesting a neuropathic rather than an ischaemic origin (Fig. 230).



FIG 231
Charcot's joints occurring in a man aged 32 years, suffering from severe diabetic neuropathy. There is gross destruction of bone and a periostitis spreading up the shaft of the first metatarsal

Neuropathic arthritis.—A destructive arthritis, closely resembling Charcot's joints in syphilitic arthritis, occurs sometimes from subacute septic infection of denervated joints It occurs in the metatarso-phalangeal and rarely in the mid-tarsal joints of the foot (Figs 231-234).

CLINICAL COURSE

Obstruction of the tibial or peroneal arteries is often unaccompanied by symptoms, and usually by the time the patient seeks advice some part of the femoral or popliteal artery is obstructed, often the femoropopliteal junction

tion of an arm been necessary in our own experience for extensive thrombosis involving the main vessels of the upper limb.

ARTERIAL OBSTRUCTION AT SPECIAL SITES

Obstruction of the abdominal aorta.—This is an unusual site of arterial obstruction from thrombosis because the pressure in and rate of flow through this vessel are both high. Sudden aortic obstruction such as occurs in embolism is a dramatic incident threatening gangrene in both limbs, but insidious thrombosis may be attended by comparatively slight symptoms. Leriche (1940)[23] drew attention to this slow thrombosis and described its outstanding features—extreme fatiguability of the lower limbs, wasting with absence of nutritional changes, pallor of the feet even on standing, and, in the male, inability to maintain an erection as a result of reduced blood flow through the pudendal arteries.

During the past seven years we have seen seventeen cases of insidious obstruction of the abdominal aorta, one of which has previously been reported.[24] The age incidence in these cases has been between forty-seven years and seventy-nine years; twelve have occurred in males and only five in females; a similar age and sex incidence has been recorded by other writers.[25] Morel (1943)[26] has reported a case at the age of twenty-nine years.

Most of our patients complained of claudication in the gluteal region, thigh or leg, or all three, and only one of aching and fatigue in the legs. Nocturnal cramps were common. Coldness, muscular wasting, paraesthesiae, indolent ulcers, colour changes and gangrene were all seen in the disease. Impotence was present in all our male cases. Swelling of the limbs has been reported.[27] Only one of our patients presented initially with hypertension.

It is surprising the length of time that can elapse before serious trophic changes occur in the limbs. In a recent report[25] of eleven cases one patient had had symptoms for eleven years and two for seven years, although the authors do not suggest that complete aortic occlusion had been present all this time. We have seen one case in which bilateral claudication had been present for six years; at the end of this time above-knee amputation of the right leg was performed for persistent pain and digital gangrene. The aorta was obstructed immediately below the renal arteries (Fig. 235). The stump healed slowly and at the present time, four years later, the left leg remains free from serious trophic change.

It appears that, although sometimes encountered, Leriche's syndrome is not always present in its entirety. Claudication, rubor on dependancy, cyanosis, swelling and trophic changes are all frequently present, but in variable combination. Furthermore, interference with erection although usual is not invariable.[27]

In the younger age group from forty to fifty-five years obstruction of the aorta is often complete, and there is frequently no evidence of gross atherosclerosis in the other vessels, but in the older age group above sixty, obstruction

Intermittent claudication is the presenting symptom in about 80 per cent. of patients, for the collateral vessels around a short obstructed segment of artery convey a sufficient blood supply for nutrition of the skin.

Frequently coldness, and often numbness, are associated with the claudication. Rarely, particularly in those who by virtue of age or intercurrent disability are unable, or sometimes unwilling, to exercise to the extent that claudication would be a complaint, a patient will present with an unhealed ulcer, persistent digital sepsis or even digital gangrene. In these circumstances, trauma is usually the precipitating factor of the local condition.

There may be no further arterial thrombosis for many years, but at any time it may occur, often as the result of injury, operations or illnesses and sometimes without apparent cause. Rarely thrombosis is extensive from the outset and massive gangrene of a leg or foot may occur, but gangrene of the thigh is exceedingly rare.

Alimentary lipaemia has been found to increase the coagulability of the blood,[20] and there may be an association between thrombosis in atherosclerosis and the ingestion of a fatty meal; it is well recognised that coronary artery thrombosis may follow such a meal.

In atherosclerotics of more than sixty years of age, it is quite probable that death from myocardial infarction or cerebrovascular accident will occur before gangrene of the limb.[21] Ischaemic heart disease is present in 40 per cent. of patients with claudication.[22] When the disease first gives rise to symptoms in the fourth and fifth decades, especially when intimal disease is at first limited, as it often is, to the femoropopliteal region, there may be little or no coronary artery disease. Life is therefore not in such jeopardy, and there is more time for progression of thrombosis in the limb. In these patients serious ischaemia or gangrene is likely to occur. On the other hand, many younger patients with a solitary femoropopliteal thrombosis suffer no further vascular incident for many years.

Both lower limbs are usually affected, though not necessarily symmetrically either as regards time or site of thrombosis. If one limb develops gangrene, there is a 40 per cent. chance that the other limb will develop gangrene, but many patients live for some years with one leg amputated and the other, though the site of claudication, yet with no severe trophic change.

Provided proper care of the feet is instituted, and if the patient takes the greatest care to avoid injury and especially burns, gangrene may be prevented for many years.

Atherosclerosis with obstruction is rare in the upper limbs. We have seen severe intermittent claudication in a patient with obstruction of the subclavian and upper part of the auxillary artery, and we have seen Raynaud's phenomenon in the hand of a man with an obstructed brachial artery. Raynaud's phenomenon sometimes occurs when the vessels are narrowed rather than obstructed by atherosclerosis. On only one occasion has amputa-

of the aorta is often partial, frequently with gross atherosclerotic changes elsewhere. Often in the latter group the bifurcation is involved by a spread of thrombosis from one common iliac artery to involve the contralateral common iliac artery



FIG. 236

Gangrene of both legs in a female patient of 78 years. At autopsy there was an old occlusion of the abdominal aorta, and a recent thrombosis of both iliac and femoral arteries. She had been confined to bed with bronchitis prior to the recent thrombosis

The *diagnosis* is not difficult provided it is considered. Bilateral claudication in the buttocks and legs is very suggestive. Premature fatigue associated with wasting of the lower limbs should lead to examination of the femoral pulses which are impalpable. Paraesthesiae, numbness, coldness and sometimes burning pain in the feet with aching pain particularly at night are suggestive of a vascular cause. Rest pain in both legs relieved by dependancy occurs occasionally and may be complicated by swelling (Fig. 236).

All cases eventually develop gangrene of the feet, often precipitated by some form of trauma. Figure 237 shows superficial gangrene precipitated by an intravenous infusion into the saphenous vein at the ankle joint after gastrectomy in a patient with thrombosis of the abdominal aorta. Thrombosis at or about the aortic bifurcation may not spread and the outlook for life of the limbs may be good at any rate for some years, but gangrene is always a danger and frequently complicates intercurrent disease. If there is extension of thrombosis upwards the renal or coeliac arteries may be obstructed with fatal outcome, and if thrombosis spreads downwards the returning collaterals are often obstructed, leading to gangrene in the limbs. We have recently seen a female aged seventy-eight with bilateral gangrene of the legs, autopsy revealing a recent thrombosis extending from the popliteal arteries below to the bifurcation of the aorta from which point up to and including the right renal artery, there was an old organised thrombus (Fig. 236)



FIG. 235
In spite of obstruction of the aorta just below the renal arteries (not well shown in the X-ray) the iliac vessels are well filled via collaterals

it may so weaken the wall of the aorta as to result in rupture. We have unfortunately suffered this experience. Re-inforcement of the anastomosis by



FIG 238
A graft would be hazardous The distal vessels are very small, and the aorta is obstructed to a point immediately below the renal arteries

fascia lata or other material has been suggested in such circumstances[30] but it might be wise not to undertake a graft when calcification is so extreme.

Disobliteration, or removal of diseased intima (p. 397), of an obstructed aorta and its bifurcation has been practised with good results,[31] but there

TREATMENT.—Before active surgical treatment of aortic obstruction is undertaken, it must be remembered that patients with this complaint may suffer little apart from some claudication, and that many retain their limbs in a reasonably healthy condition for long periods without gross disability. Furthermore there may well be disease and obstruction in the distal vessels of the limb, and this must be considered before treatment is started. In the

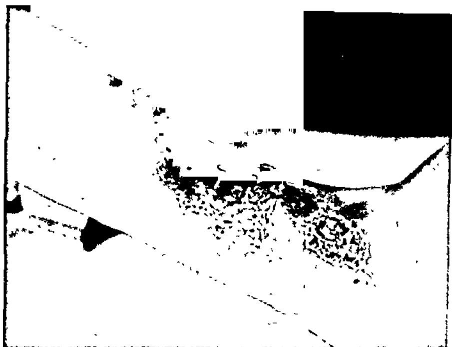


FIG. 237
Painful gangrenous ulcer arising at the site of an intravenous infusion after gastrectomy in a patient with obstruction of the abdominal aorta.

younger age group when obstruction is localised to the region of the bifurcation, and when there is no significant atheroma apparent elsewhere on arteriography, excision of the obstructed segment and replacement by a suitable graft is an operation accompanied by excellent results.[28, 29] In the older age group when the bifurcation has become obstructed by a " spread " of atherosclerosis and thrombosis from one common iliac artery to involve the bifurcation, the excision of thrombosed vessel may have to be so extensive as to preclude attempts at grafting (Fig. 238). Provided thrombosis has not spread upwards to involve the aorta immediately distal to the renal arteries, a graft may be inserted We are averse to attempt a graft when the distal anastomosis would have to be done below the inguinal ligament, and the presence of obstruction in the distal vessel must always be considered, though DeBakey has successfully inlaid grafts from renal arteries to popliteal fossa Difficulty may be encountered in stitching a graft when calcification is advanced and it may be impossible to insert the needle, bearing fine sutures, through the vessel wall, and although removal of the calcium plaque will enable this to be done,

obliteration gives rise to claudication of the calf muscles and coldness of the foot. In the early cases trophic changes are absent or minimal, and the skin of the feet is healthy. There is pallor on moderate elevation of the limb and in later cases rubor on dependancy, the foot regaining its normal colour when horizontal. The popliteal pulse and pulses below this level cannot be felt but often collateral vessels can be palpated over the medial and less often the lateral condyles of the femur. Provided there is no spread of thrombosis, and that the limb is protected from injury the prognosis as regards gangrene is good and in the elderly death from coronary disease or other cause will in the majority precede this.

Obstruction of the tibial and peroneal vessels.—Obstruction of one of these vessels is generally symptomless, although a long obliterated segment of the posterior tibial artery may result in claudication of the foot muscles, and occasionally of the calf muscles, some of whose blood supply is drawn from this artery. Obstruction of the peroneal artery is unusual. A Raynaud's phenomenon in the foot is not infrequent when two of the three vessels are affected, and trophic change or gangrene is highly probable if all three vessels are obstructed.

Obstruction of the vessels of the foot and toes.—A Raynaud's phenomenon, claudication of the foot muscles, and later trophic changes, persistent colour changes and finally severe rest pain and gangrene occur. Atherosclerosis of the digital vessels does not occur, though local thrombosis may be seen (p 331).

Obstruction of the subclavian arteries.—Because of the excellent collateral circulation, especially if the obstruction is distal to the origin of the thyrocervical axis, symptoms may be entirely absent. On the other hand, we have seen a severe Raynaud's phenomenon in the fingers, together with pallor on elevation of the arm and intermittent claudication and wasting in the forearm and hand muscles in a female patient of sixty-five with atherosclerotic obstruction of the subclavian artery. A severe ache as opposed to a cramping pain in the shoulder and arm muscles, occurring after exercise is said to be characteristic. Atherosclerotic obstruction of the vessels of the arm, forearm and hand is rare, although tortuous calcified vessels are common. We have only seen one patient with massive gangrene of the arm, requiring amputation, and there was in this case absence of pulsation in the subclavian arteries, and on examination of the amputated limb all the main vessels of the arm and forearm were filled with ante-mortem clot

Special Investigations

Radiology.—Radiology of the soft parts may reveal calcification in the arteries of the limb, particularly in the aorta and iliac vessels, yet its absence is not significant. The significance of calcification in arterial obstruction has

appears to be considerable risk of haemorrhage from the suture line in the vessel, unsupported as it is by surrounding muscles. Reinforcement by fascia lata graft may be wise.[30] In some series, the mortality rate has been rather high.[32]

Sympathectomy appears to be of some value in aortic obstruction, and should be considered in the presence of trophic changes in the feet.[27, 33, 25] In order to avoid injury of important collateral vessels, the operation should be done transperitoneally through a midline incision and the first lumbar ganglia should be removed,[25] though this may be difficult through such an incision.

Resection of the thrombosed segment of the aorta has been advocated[23, 33] but difficulty may be experienced in closing this large vessel, and there seems to be little to be gained from the procedure.[25]

OBSTRUCTION OF THE COMMON AND EXTERNAL ILIAC ARTERIES

Obstruction of these vessels occurs most commonly at the origin of the common iliac artery from the aorta. Both vessels have a free collateral circulation, and the clinical features of obstruction of the common or external iliac arteries are very similar. They consist of pallor of the foot on exercise, intermittent claudication or aching and fatigue of calf and often thigh and gluteal muscles, and usually absence of trophic changes in the feet. The pulse of the femoral artery is frequently palpable, though diminished and sometimes delayed.[34] Symptoms are less severe where the obstruction is in the common iliac artery, because of the existence of a very free circulation via the hypogastric arteries across the pelvis. Ten cases of obstruction or partial obstruction of the common iliac artery occurring in fifty-three consecutive cases of intermittent claudication have recently been reported,[35] but this is in our experience an unusually high incidence, although the obstruction at these sites as a result of atherosclerosis is not uncommon.

The occurrence of intermittent claudication in the presence of palpable pulses has been attributed to " spasm " of arteries—spastic claudication[36, 37]—but it seems probable that a further search in similar cases might reveal an obstructed iliac artery.

TREATMENT.—This is based on principles similar to those discussed in aortic obstruction. Sympathectomy is of some value.

OBSTRUCTION OF THE FEMORAL AND POPLITEAL ARTERIES

These arteries are the commonest vessels to be affected by atherosclerosis, and the process begins frequently at one of two sites—behind the knee joint or, more usually, at the adductor opening. There is as always a tendency for the process to extend from these levels upwards or downwards or both Extension from the adductor opening more commonly occurs upwards into the femoral artery, leaving the popliteal artery patent. Femoropopliteal

obliteration gives rise to claudication of the calf muscles and coldness of the foot. *In the early cases* trophic changes are absent or minimal, and the skin *of the feet is healthy.* There is *pallor* on moderate elevation of the limb and in later cases rubor on dependancy, the foot regaining its normal colour when horizontal. The popliteal pulse and pulses below this level cannot be felt but often collateral vessels can be palpated over the medial and less often the lateral condyles of the femur. Provided there is no spread of thrombosis, and that the limb is protected from injury the prognosis as regards gangrene is good and in the elderly death from coronary disease or other cause will in the majority precede this.

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Special Investigations

Radiology.—Radiology of the soft parts may reveal calcification in the arteries of the limb, particularly in the aorta and iliac vessels, yet its absence is not significant. The significance of calcification in arterial obstruction has

been discussed elsewhere (p. 243). It suffices to re-emphasise the importance of distinguishing between medial calcification, or Monckeberg's sclerosis, of little or no significance as regards arterial narrowing and obstruction, and intimal calcification, which is of much more importance in this respect. X-rays of the feet may show osteoporosis and sometimes osteomyelitis from infection from an overlying ulcer, and the presence of the latter would influence the decision in favour of amputation in certain patients. Arteriography gives a precise picture of the site and degree of arterial disease, but is neither necessary nor justified in many cases as the clinical features indicate very accurately the pathology present. It is however of use in the following circumstances:—

1. In cases of obliteration of proximal arteries, where local operative procedures may have a place, particularly where disease of the aorta, iliac and femoral vessels is suspected.
2. Prior to certain amputations, to determine the probable blood supply of skin flaps.

Examination of the blood.—This is an exceedingly important investigation in the evaluation of any patient with ischaemic symptoms, for anaemia is common in elderly and debilitated patients, and the correction of this is an important factor in treatment. A fasting blood sugar estimation should be made, in addition to the routine examination of the urine for sugar. The estimation of the plasma lipoids may be valuable as it is said that increased values, more than 650 mg. per 100 c.c. of plasma, are indicative of atherosclerosis rather than other causes of vascular obstruction.[38]

Laboratory tests of the circulation.—Estimations of blood flow in a limb are discussed fully elsewhere These methods are of great scientific interest, but influence the treatment little.[39] Tests to determine the probable effect of sympathectomy are unreliable as sympathectomy always produces more vasodilatation than would be expected from any pre-operative test. Of all the methods available, local anaesthetic block of the posterior tibial nerve at the ankle joint with plethysmographic estimation of the blood flow gives the most accurate forecast of the results to be expected from sympathectomy.

DIAGNOSIS

Intermittent claudication, colour changes either postural or persistent, unilateral coldness of a foot, inability to feel a pulse in the region of the ankle joint (allowing for the occasional congenital absence of the dorsalis pedis artery) all suggest arterial obstruction Before muscle ischaemia gives rise to the more usual cramping pain, excessive fatigue may be experienced, though this is rapidly relieved by rest. Ischaemia of the thigh, gluteal and shoulder muscles is more often an ill-defined aching than a cramp, and has not infrequently led to a diagnosis of sciatica or arthritis[40] Claudication in the foot muscles has often been diagnosed as foot strain.

The pa [illegible] such a precise clinical syndrome that it is [illegible] st unlikely to be present in the calf if [illegible] or tibial pulses are full and bounding It can, however, occur in the presence of these pulses in cases of severe *anaemia*[53] (*Fig.* 239), in coarctation of the aorta[42] and in obstruction of the iliac arteries[54, 55] and may also occur in localised disease of one vessel supplying a muscle or part of a muscle, as occurs in the gastrocnemius whose artery of supply is often an end-artery. It is occasionally present in a patient with incomplete obstruction of the femoropopliteal artery.



FIG. 239

This female patient of 76 years complained of angina of effort and intermittent claudication of the calf muscles after walking about ten yards. She was intensely anaemic and always wore a lace cap which hid the tumour of her scalp. This tumour was ulcerated Removal of the tumour led to recovery from her anaemia and relief of her angina and claudication.

As a result of persistent ischaemia a coarse fibrillation of muscle, well seen in the adductor hallucis, may occur spontaneously when the limb is at rest and if associated with tenderness is very suggestive of ischaemia.

Digital ulcers and gangrene may give rise to difficulty, and in *diabetic neuropathy* they may occur in spite of a blood supply otherwise adequate for life of the part. In many cases of diabetic gangrene pulses at the ankle joint are present, and atherosclerosis can be excluded, as this disease usually does not involve the vessels of the feet unless the larger vessels of the leg are also obstructed. Colour changes and pain are absent in diabetic neuropathic gangrene. However, in many such cases there is an associated arterial degenerative process, with ischaemia which itself would not be sufficient to cause death of tissue in the non-diabetic, and it is important to *recognise the* type for conservative treatment or local amputation may well be effective.

Digital gangrene in *acrocyanosis* and *livedo reticularis* is often multiple involving skin only or perhaps a terminal phalanx. Wasting of the subcutaneous tissues of the digits and often rarefaction of the phalanges is present. There is a long history of " poor circulation " in all the fingers and toes and often of chilblains, and distal pulses are usually palpable. The prognosis in these conditions is invariably good, and sympathectomy is valuable.

When arterial obstruction is present in a patient over fifty years of age, atherosclerosis is the cause in almost all cases. Findings contributing to the diagnosis but not necessarily present include hardened, irregular, tortuous vessels, intimal calcification on X-ray examination and irregularity of the lumen of the vessels on arteriography, although in early cases this may not be evident. In younger patients in the third and fourth decades, an isolated obstruction of the femoropopliteal artery may give rise to great difficulty in diagnosis. Boyd[21] considers such cases to be traumatic in origin, but on prolonged observation of similar cases, some, particularly those occurring in the third decade, develop further arterial and venous occlusions typical of thromboangiitis obliterans, and others, particularly in the fourth decade, develop similar major vessel lesions in the other limb with evidence of intimal irregularity in other parts of the vascular tree seen in arteriography, and in those a diagnosis of atherosclerosis can safely be made.

A history of recurrent superficial phlebitis, and involvement of the upper limb as well as the lower limb suggest *thromboangiitis* rather than atherosclerosis. A Raynaud phenomenon in the fingers is common in thromboangiitis and rare in atherosclerosis.

In sudden arterial occlusion, particularly when occurring as a first sign, *embolism* must be suspected, but absence of an apparent source of such an embolus, makes a diagnosis of embolism improbable, especially in a patient more than fifty years of age, and suggests an acute thrombosis of an artery the site of atherosclerosis.

TREATMENT OF ATHEROSCLEROSIS

Treatment of acute ischaemia of the limb.—Acute ischaemia may result from thrombosis of a vessel the site of atherosclerosis and the clinical signs and symptoms may be indistinguishable from those accompanying embolism or other sudden occlusion of the arteries.

Treatment consists of anticoagulant therapy, rest in the optimum position, the avoidance of extremes of temperature, and measures to increase the quality and quantity of the blood flow to the part.

Heparin is given as a matter of urgency, and delayed clotting of the blood is maintained by tromexan for four weeks, for short segments of thrombosed arteries may recanalise completely after prolonged tromexan therapy.[43]

Rest in the optimum position is achieved by raising the head of the bed on 9″ blocks thereby taking advantage of gravity to assist blood flow

whilst avoiding stasis and swelling which would result from greater dependency. In the presence of any swelling, the bed should be level.

The affected limb should be kept cool, *i.e.* at ward temperature, not cold as has been suggested, for this may interfere with the dissociation of oxyhaemoglobin and also result in local vasoconstriction. The leg is left uncovered by bed clothes and exposed to the atmosphere of the ward, usually about 22°C. Hot water bottles must of course be avoided, as burns may readily occur from the diminution of sensory acuity which may be present in the limb

If anaemia is present this must be treated, and a blood transfusion is given if necessary, and if thrombosis has occurred after operation, injury or illness, any associated hypotension must be corrected. Post-operative and post-infective dehydration must be prevented.

Methods of increasing the blood flow through collateral channels are those which decrease sympathetic tone, *i.e.* bodily warmth, deep sleep and vasodilator drugs. The patient's trunk and unaffected limbs should be warmed by blankets, hot water bottles and hot drinks. Deep sleep is encouraged by the use of suitable barbiturates, and alcohol not only encourages this but is a valuable vasodilator as well. The only drug we have found to be of value is priscol, given intra-arterially, above the site of obstruction in doses of 50 or 75 mg., but we are averse to the repeated puncture of an artery for fear of local thrombosis and only one or two doses are given by this route. It may be valuable to repeat the dose at four-hourly intervals by intramuscular injection Sympathetic block by paravertebral injection of local anaesthetics is not advisable in a patient undergoing anticoagulant therapy, as the most alarming retroperitoneal haemorrhage may occur, and it should not be necessary as the non-operative measures achieve a very substantial release of sympathetic tone for the few days which elapse before the fate of the limb becomes clear. For a similar reason resection of the sympathetic trunk is not done in the acute stage of the disease. Smoking is prohibited.

Treatment of chronic ischaemia of the limb.

GENERAL CARE OF THE PATIENT.—Patients suffering from atherosclerosis are usually elderly, many with coronary disease, some with diabetes, and some with intercurrent disease. The patient's condition must be carefully assessed, and it is particularly important to correct anaemia as the health of the distal tissues depends as much on the quality as on the quantity of blood received. Many elderly patients, and particularly those who have associated diseases, suffer from hypoproteinaemia and a high protein, high calorie diet is important. The atmosphere of gloom often surrounding a patient with threatened or manifest gangrene must be dispelled to be replaced by an encouraging outlook and a frank explanation of an orderly plan of treatment, the objects of which the patient can understand.

Measures to arrest the progress of the disease.[41]—There is considerable evidence that hypercholesterolaemia and increased or abnormal lipoproteins

in the plasma may in some measure be a cause of atherosclerosis, and a diet low in cholesterol has been advocated in the hope of preventing the progress of the disease. In some experimental animals excessive intake of cholesterol leads to atherosclerosis, but in man cholesterol feeding has no effect on the blood cholesterol level. On the other hand a high calorie—high fat diet generally results in a raised blood cholesterol, whereas diets which are deficient in calories and fat generally lead to a lowered blood cholesterol. Individual responses to changes in diet vary greatly, and blood lipoid levels may or may not be affected by such changes, and, as an endogenous as well as dietary sources of cholesterol exist, hypercholesterolaemia may result from metabolic disorders as well as from excessive ingestion of lipoids.

Plasma lipoids may be reduced by thyroid and iodide feeding, oestrogen injection, ACTH, feeding with brain extracts and soya bean, heparin injection and ultraviolet radiation. Starvation reduces plasma cholesterol and there is evidence that in persons of some nations subjected to near starvation during the last war the incidence of coronary thrombosis fell to unusually low levels.[45]

The problem of the aetiology and treatment of atherosclerosis has recently been reviewed by Page (1954)[44] who concludes that there is no practical way of preventing the disease, although its progress may be slowed and it is possible there are ways of aiding its resolution. He suggests in a tentative manner, the following methods which may be worthy of further trial and investigation :—

1. Iodide and thyroid administration.
2. Low calorie-low fat diet.
3. Heparin-like substances.
4. Oestrogens.
5. Dihydrocholesterol and other cholesterol analogues.
6. Brain extracts.
7. Active exercise with its massaging action on lymph flow.

Care of the ischaemic extremity.—Extremes of temperature should be avoided, and the feet must be kept scrupulously clean They should be bathed every day in water, comfortably warm. Careful drying, especially between the toes, followed by the application of spirit, and a powder consisting of equal parts of starch, boric and zinc helps to keep the skin dry and clean, and discourages fungus infection. If there is evidence of established fungus infection, the feet should be bathed in a solution of 1/10,000 potassium permanganate. They must be kept cool—not cold—and it suffices for the patient to sleep with the feet outside the bed clothes in the summer time, but in the winter they may be covered with one sheet. The toenails should be cut straight across to discourage ingrowing, and corns should not be trimmed, rather should the cause of the corn be eradicated. Salicylic acid or similar epithelial solvents must not be used. The shoes should be examined for any projecting nail or irregularity and the utmost care must be taken to avoid any injury, however trivial Any scratch or abrasion must be treated seriously, and strong

antiseptics must be forbidden Locally applied penicillin may aggravate the condition if there is skin sensitivity, but local streptomycin can be used more safely. Antibiotics are better given parenterally.

In bed at night the affected limb must not be elevated, and is best slightly dependent, a suitable position being achieved by raising the head of the bed on 9" blocks. Excessive dependency must be avoided, as it tends to encourage oedema.

Where colour changes are persistent, rest pain present and skin atrophy marked, and especially in cases of established sepsis and threatened gangrene, the patient should be confined to his bed; but if gangrene does not appear imminent and the skin and subcutaneous tissues are relatively healthy he should be allowed to get about within the limits imposed by the claudication which is almost invariably present.

If conservative treatment is to be undertaken for a patch of superficial gangrene, pus forming at the line of demarcation must be allowed to escape. The hard leathery scar frequently seen must be softened by moist dressings, and soaks twice a day for twenty minutes in warm 50 per cent. eusol are helpful The dead tissue can be cut away with scissors and it is often gratifying to find relatively healthy granulations beneath. If pus is formed, the blood supply is adequate for healing when other conditions are favourable.

Measures to increase the blood supply of the limb.—The effect of smoking on the peripheral circulation has been fully discussed elsewhere. In atherosclerosis as in thromboangiitis obliterans it should be forbidden.

Peripheral vasodilatation can be secured readily by alcohol, and within reasonable limits its use should be encouraged. The trunk should be kept warm at nights, and deep sleep induced A warm bed, a nightcap of whisky and a barbiturate all contribute to peripheral vasodilatation and in addition give rise to a feeling of well being. The use of barbiturates in acute thrombotic incidents is justified, but in chronic cases must be discrete, for the fear of addiction.

As regards tissue extracts and special drugs used specifically for their vasodilating properties, we have not been impressed with any except priscol in the early case of acute thrombosis. Tissue extracts derived from the pancreas, skeletal muscle, liver and kidney have been advised, but we can see no rationale for their use Shepherd (1950)[46] could demonstrate no increase in blood flow to the calf using an insulin-free pancreatic extract. Acetylcholine has a very transient vasodilator effect and is valueless therapeutically in atherosclerosis. Vitamin B complex has not helped in ischaemic neuritis, though of course proper vitamin therapy is part of the general treatment of the patient. There is no useful place for the nitrites, thiocyanates, or nicotinic acid in atherosclerotic ischaemia. Boyd *et al.* (1949)[47] have strongly advocated vitamin E. or alpha-tocopherol, in doses of 400 mg. daily but point out that the effect of treatment by this drug is not apparent for two months. We have tried this drug in a large number of cases, but have not found ...

be attributed to its use. Hamilton (1953)[48] has shown that there is no reason to suppose that it has any beneficial effect on the peripheral circulation.

Great interest has centred around the use of priscol in doses of 25 to 50 mg. three times a day by mouth and it appears to have some value, at least in the early stages of main vessel obstruction. Goodwin and Kaplan (1953)[49] have reported symptomatic improvement with occasional increase of claudication distance after its use, and Douthwaite and Finnegan (1950)[50] report similar results, and particularly do they emphasize its value in relieving rest pain. Lynn (1950)[51] has not been able to demonstrate any increase of blood flow on plethysmography after a dose of 150 mg. priscol daily by mouth, although there is a marked temporary increase of flow following intravenous or intra-arterial injection of the drug. The use of priscol is open to certain criticisms as its vasodilating action is general throughout the body and therefore it is possible that there is increased flow to the comparatively unaffected limbs at the expense of the flow in the diseased limb. We believe that the drug is useful in acute thrombosis, and may be of value in long-standing cases, if other methods of treatment are contraindicated, but we have not been impressed with the clinical results.

The intra-arterial injection of a variety of substances has been suggested from time to time, but few convincing reports have been made of its value. A recently conducted series of experiments has been made with the following drugs[52]:—Acetylcholine, alcohol, histamine, papaverine, tolazoline (priscol), adrenaline, hexamethonium, hydergine, cytochrome C, gallamine, triethiodide, atropin, nikethamide, curare, sodium nicotinate and procaine. The investigators estimated improvement by clinical, oscillometric and claudicometric standards and found that priscol and papaverine were effective, and that the latter drug was less likely to produce distressing side effects than the former Kinmonth (1952)[54] in a study of arterial spasm was however unable to demonstrate any vasodilating effect of intra-arterial papaverine. The whole question of intra-arterial therapy is on trial, but we are averse to repeated arterial puncture in cases of atherosclerosis and are not impressed with the value of such therapy.

Various physical methods of increasing blood flow in a limb have been advocated, such as intermittent venous occlusion, the use of an oscillating bed, and Buerger's exercises. These measures depend on rhythmic diminution of blood flow with a resultant secondary hyperaemia of the part. The use of intermittent venous occlusion has been investigated by Thompson and Vane[55] and they have shown that the increase in blood flow is only transient and is not sufficient to compensate for the period of induced diminution of flow. These methods therefore may possibly be harmful, but Buerger's exercises may have some psychological value.

Sympathectomy of the affected limb remains the most valuable method of improving blood supply[53, 55 21, 56] although it in no way affects the progress of the disease. Longland[56] has demonstrated the increase in diameter of

collateral vessels of the rabbit following sympathectomy. Lynn and Barcroft[58] have shown that immediately after sympathectomy in the non-atherosclerotic, the blood flow may increase seven or eight fold in that limb, but recovery of tone occurs rapidly so that at the end of two weeks the flow is only about twice the pre-operative level, though it remains at this level for an indefinite period. In the atherosclerotic limb the picture is similar, but although the original increase of flow is not so great because of the degree of vascular obliteration which is present, there is a permanent increase of flow which remains about twice the pre-operative level. The effect of sympathectomy cannot be predicted from pre-operative tests.

As a result of sympathectomy the limb becomes permanently dry with consequent inhibition of fungus infection. It becomes warmer, both objectively and subjectively and the increased blood flow, most marked in the digits and foot frequently leads to the healing of ulcers, the separation of small gangrenous patches and the relief of mild rest pain. When amputation of a single toe is contemplated, this is rendered a safer procedure if a sympathectomy is done, preferably at the same time as the amputation, for blood flow is maximal just when healing commences. A golden opportunity may well be lost if the sympathectomy is done some time before the amputation, as has been advocated, for by this time there will have been return of some degree of tone in the distal vessels when the local amputation is performed. Sympathectomy improves or relieves intermittent claudication of the calf muscles in about 20 per cent. of cases, but it may be a year before the benefits of the procedure are apparent. This delay may be due to the time required for the full development of the collateral circulation. Relief of [illegible] is more [illegible] the gastrocnemius. It is wise to warn the patient that the pain of claudication is unlikely to be greatly relieved, but that the nutrition of the feet will be improved, coldness of the extremities will disappear, and the possibly serious effects of minor trauma will be lessened. The vasoconstrictor effect of smoking is perhaps absent in the sympathectomised limb.[59]

Calcification and tortuosity of vessels are no contraindications to operation, and indeed often most satisfactory results are obtained even when these are demonstrable.

Indications for sympathectomy.—Dornhorst[60] whilst not satisfied with the results considers that the operation should be advised in all cases of material disability unless the general condition of the patient forbids it. Learmonth and Slessor[61] consider the operation most effective in cases with small ulcers or gangrene limited to the distal phalanges, but do not limit the procedure to this type of case. Boyd[31] considers that sympathectomy remains the mainstay of the treatment of obliterative vascular disease of the limbs. Kvale[62] states that surgical sympathectomy is the method of choice. [illegible]

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operation should be done only in those under sixty years of age, but age itself appears to be no bar to the operation, and we have operated on patients of seventy-five years with, we believe, prevention of gangrene and definite subjective and objective improvement. There seems to us no reason for denying the benefit of operation on grounds of age alone where the condition of the patient otherwise warrants the procedure. Sympathectomy is certainly the most effective treatment available and should be advised except:—

1. when coronary disease or intercurrent disease makes the procedure dangerous;
2. in diabetics with atherosclerosis when the degree of neuropathy is such that the sympathetic fibres have degenerated, in which case the diabetes has in fact produced a sympathectomised limb; these cases can be detected by absence of vasodilatation in the digits after heating or cooling of the trunk (p. 376).
3. in the presence of gangrene of the foot; gangrene of a toe, provided the proximal part is not pre-gangrenous nor the site of spreading infection, is no contraindication, and amputation of the toe should be performed at the same time;
4. in the presence of severe rest pain in association with persistent colour change—a pre-gangrenous condition; mild rest pain is often relieved by sympathectomy and if such pain can be relieved by non-operative vasodilating procedures, rather than by alleviant drugs, such as morphia or pethidine, it will be relieved by sympathectomy;
5. in the presence of associated oedema of the foot; in these cases sympathectomy may precipitate gangrene, possibly due to " increasing oedema about the proximal limits of the doubtful area ",[63]
6. when symptoms are not severe enough to warrant the operation; many patients do not complain of claudication until after 400 yards or so, do not show evidence of distal ischaemia, and do not suffer from coldness of the foot; in such cases if the obstruction is in the lower part of the femoral artery it is probably wiser not to advise sympathectomy, as the claudication will probably not be significantly improved by the operation, as it may be if the obstructon is in the upper part of the femoral artery;
7. when there has been recent acute thrombosis; it is better in such cases to treat the patient on conservative lines until the fate of the limb is known; sympathectomy may be reconsidered again then.

The results of sympathectomy are disappointing in patients with obstruction of the aorta, its bifurcation, or one or both iliac vessels, and there is no certainty that improvement will follow operation. It is better to increase blood flow by a grafting operation if possible, but if at laparotomy it is found that grafting is impracticable, then a sympathectomy should be done in the hope that it will be of some value.

In patients who are advised to have sympathectomy, the operation should be done on both sides at the same time, on the presumption that the disease is bilateral. There is no added risk, and the operating time is little prolonged.

As regards the extent of the operation of lumbar sympathectomy, there is not complete agreement. There appears no doubt that complete denervation of the lower limb requires removal of the first, second and third lumbar ganglia, and if the operation is done for obstruction of the iliac arteries, or the upper half of the femoral artery, the first ganglion together with the second and third should be removed. If the obstruction is below the level of mid thigh, it has been suggested that denervation of the whole limb may rob the distal part of the limb of blood by opening up the vascular bed in the proximal part,[64] an incident seen in iliac block where diversion to the proximal part on exercise is accompanied by pallor of the foot. Leriche (1933)[65] advises removal of the second and third ganglia only, and this is also the extent of the operation recommended by Telford (1947).[66] It is our practice to remove the second and third lumbar ganglia when the obstruction is at or below the femoro-popliteal junction, and to remove the first ganglion as well when the obstruction is above this level.

When the age and general condition of the patient is such that operation is inadvisable, the paravertebral injection into the lumbar sympathetic chain of 10 c.c of a 10 per cent. solution of phenol in water results in a dry and warm foot for a long time.[67] Before the injection of the phenol 2 ml. of 4 per cent. procaine is injected through the needle and the temperature of the foot is observed to ensure that the point of the needle is properly placed, for injection of the phenol solution into the neighbourhood of a somatic nerve results in paralysis, or in persistent pain referred distally and due to perineuritis[60] Examples of paraplegia after injection of phenol have occurred when the needle has entered the sub-arachnoid space. It is a dangerous treatment, and not recommended

Other surgical measures to increase blood flow.

ARTERECTOMY.—Leriche[21] has maintained that an obstructed segment of artery acts as an irritative focus which originates a reflex arc causing spasm of the vessels of the limb, and he advocates excision of the affected segment. Good results have been reported after this procedure, but Leriche's concept has not been generally accepted in Britain, and the surgical approach and excision of the blocked segment may require division of important collaterals

"DISOBLITERATION" OPERATIONS.—Dos Santos[68] in 1947 described an operation for removing intraluminal clot from thrombosed vessels together with intima and inner media, and Reboul and Laubry (1950)[23] have performed the operation on the aorta and on the peripheral vessels, under the cover of adequate heparin therapy, and quote 38 per cent successful results,

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The variation in the selection of patients for operation, and the different criteria for assessment are reflected in the variability of reported results.[73, 74, 75, 76]

If those patients are selected who have a reasonable collateral circulation already established, then the operation will give significant relief of symptoms and will result in improvement of the nutrition of the skin of the feet, and after all it is gangrene which is the most sinister complication to be avoided, but if the operation is done for those with such a degree of arterial occlusion that gangrene is probable, then sympathectomy can achieve little, although it may postpone the day when amputation is necessary. Age, or diabetes in the absence of neuropathy, does not affect the results of sympathectomy.

The treatment of pain in atherosclerosis.

INTERMITTENT CLAUDICATION.—The effect of sympathectomy on claudication is discussed above. Where there is gross interference with the blood supply to a muscle, or group of muscles, wasting occurs, and therefore a claudicating muscle which shows clinical wasting will not sustain a significant increase in blood supply after sympathectomy and the pain of intermittent claudication will not be relieved.[64]

Denervation of claudicating muscles has been suggested,[61] and can be simply done by division of the nerves to the medial and lateral heads of the gastrocnemius through an incision in the popliteal fossa, but the results in our hands have been disappointing and we have abandoned the operation. On the other hand denervation of the anterior tibial muscles, in those rare and often severe cases where this muscle group is the site of pain, is very effective. It can be achieved by crushing the lateral popliteal nerve as it winds round the neck of the fibula. After this, foot drop occurs, and a toe spring is necessary.

Division of the tendo Achillis has been advocated[67] and has a useful place in those cases of claudication where pain is so severe as seriously to interfere with walking more than fifty yards. The condition of the skin and subcutaneous tissues of the foot must be reasonably healthy to withstand the extra work imposed by an increased walking distance. We have a number of patients on whom we have done this operation bilaterally and who can now walk slowly for a mile or more without pain. There is a marked tendency for the tendon to reunite by fibrous tissue, and the operation may have to be repeated on more than one occasion,[77] but if the division is made at a rather high level, about 2″ above the tendon's insertion into the os calcis, reunion seems less likely. Both sides can be operated on at the same time, and although there is some unsteadiness at first [illegible]
to bal[illegible]
still o[illegible]
be dor[illegible]
activit[illegible] [illegible] deficiencies.

the vessels remaining patent. Others have reported successful results following "disobliteration"[69, 30, 70] of the aorta and its branches, and also of the peripheral vessels. With a comparatively short length of major vessel, such as the aorta, or iliac artery, obstructed by thrombosis, removal of the intraluminal clot may be considered, but we have seen rupture of the aorta after this procedure, and very early re-thrombosis of limb arteries which have been "disobliterated." In one series of cases there was a 12 per cent. mortality rate, most of the deaths occurring when the intra-abdominal vessels had been operated on.[32] Aneurysms may also follow.[71]

Many of the cases which have been chosen for the procedure would have been suitable for a vessel graft.

We have not been at all satisfied with "disobliteration," and it seems at the moment that the procedure in its present form is not a useful surgical manoeuvre.

ARTERY GRAFTING.—There is a limited place for excision of thrombosed segments of arteries and replacement by grafts of vein, artery or other material. The question of the indication for and methods of artery grafting will be discussed later.

LIGATION OF THE FEMORAL VEIN.—Ligation of the femoral vein has been advocated,[72] but it does not appear to be a rational procedure, and might increase congestion and swelling of the limb.

Results of sympathectomy.—It is difficult to classify the result of sympathectomy as good, fair or bad in the individual case unless a clear understanding of what is to be expected is shared by the patient as well as the doctor. It is, for example, disappointing for all concerned if the operation is done on a patient with incipient gangrene associated with extensive arterial obstruction. Intermittent claudication, the most frequent first complaint in the course of the disease, is the symptom, short of incipient gangrene, which is most difficult to relieve. Favourable cases are those which result from a short segment of obstruction in the upper half of the femoral artery, and of these about 75 per cent. will be relieved or cured. When the obstruction is in the region of the femoropopliteal junction, relief is much less certain, and only about 20 per cent of patients will admit improvement of claudication and in these it may be a year before improvement occurs, a fact of which the patient should be warned.

Early trophic changes, paraesthesiae, coldness and numbness will almost invariably be relieved completely by the operation, and distal ulcers and small patches of digital gangrene, provided the adjacent tissues are not pregangrenous, will heal in the great majority.

Rest pain, if relieved by medical measures, will be relieved by sympathectomy, but if a prelude to gangrene and only relieved by pain-relieving drugs will be uninfluenced by the operation, and patients with such symptoms should not be advised to have the operation.

The treatment of gangrene.—The object of the treatment of gangrene is the removal of dead tissue, with healing of the adjacent part. The key to the problem lies in the ability of proximal tissues to heal, and this depends not only on the blood supply, but also on the presence of constitutional factors such as diabetes, anaemia and the general condition of the patient. The control of diabetes, the correction of anaemia and attention to the nutrition and hydration of the patient are factors of the utmost importance.

It is not the site of the gangrenous part which necessarily dictates the extent of removal, and the essential consideration is not the dead, but the adjacent living tissue. If the tissues immediately proximal to the gangrenous area have an adequate blood supply, then amputation can be local, but if these tissues are severely ischaemic, and unable as a result of this to complete the process of repair, then a higher amputation through tissues with a sufficient blood supply is demanded. The state of the tissues adjacent to the gangrenous part can be estimated by their associated symptoms and clinical appearance. Severe rest pain, rubor or cyanosis which persist in spite of alterations in posture, extreme pallor which is maintained after dependency for one minute and severe atrophy of skin and subcutaneous tissues, all indicate ischaemia of such severity as to render healing improbable if amputation is performed through such tissue. Swelling renders healing of such tissues improbable, but if the swelling is due to infection it may sometimes be reduced by the use of antibiotics; local amputation may then be considered. Mild rest pain does not necessarily preclude a local amputation, and if the clinical evidence does not reveal ischaemia of critical severity, then removal of digits may be justifiable, especially if a lumbar sympathectomy is done at the same time, but usually amputation through tissue the site of rest pain is not successful. If gangrene has occurred, a line of demarcation should be awaited, but as soon as this has formed, dead tissue is removed, although minor gangrene involving the skin alone can be allowed to separate by natural means (*vide infra*).

Embolic gangrene in atherosclerosis results from single or multiple small emboli arising from proximal thrombosis and may result in gangrene of a digit or in multiple areas of cutaneous gangrene. In these circumstances, the circulation in adjacent parts is well maintained and therefore removal of tissue or amputation through or just proximal to the line of demarcation will usually heal. On the other hand gangrene occurring as the result of distal thrombosis from injury or sepsis may demand a major amputation as thrombosis often spreads into the proximal tissues. Severe and intolerable pain, if not resulting from sepsis when it may be relieved by suitable measures for the relief of tension, demands a major amputation, even when frank gangrene is not present. In these circumstances there is other evidence of critical ischaemia; major amputation should not be unduly [illegible]

[illegible]

mini[illegible]

[illegible] of emboli arising

Injection of long acting local anaesthetics into the muscle originating the pain sometimes gives relief for a few weeks or months, and we have used proctocaine in amounts of 10 ml. for this purpose. As a simple out-patient procedure it is sometimes useful when there is localised tenderness in the affected muscle, but it is by no means always successful.

The use of a check iron to prevent movement at the ankle joint is a useful measure giving considerable relief[8] and further experience may indeed prove it to be a most valuable palliative measure in the symptomatic treatment of intermittent claudication.

Rest pain.—Ischaemic rest pain is a symptom of incipient gangrene but even the smallest increase in the blood supply may be sufficient to relieve it, and sympathectomy is often surprisingly effective. If, however, pallor, rubor or cyanosis is persistent in spite of posture, the circulation is stagnant and little relief can be expected from any vasodilating procedure. As the intensity of the pain appears to vary with the degree of ischaemia, it is a useful and valuable indication of the effect of any treatment. The pain is not confined to any particular nerve territory, and such measures as nerve crushing or section, blocking by alcohol or long acting anaesthetics are of insufficient value to merit a place in the treatment of ischaemic pain Pain will diminish as the blood supply to the part is improved, and conversely its persistence or increase is an indication for amputation, a measure which should not be delayed unduly. Those patients whose pain is relieved by non-operative measures designed to produce vasodilatation should be advised to have sympathectomy.

Ischaemic pain associated with sepsis.—Frequently a subungual extension of a paronychial infection gives rise to rest pain of great severity, and relief of the tension of the sepsis relieves the pain. It is by no means always apparent that there is pus underlying the nail, frequently that of the great toe, but close examination of the paronychial folds will reveal localised redness, tenderness or swelling, and any pressure on the nail will be exquisitely painful. The relief of tension in such a case is a difficult problem. Avulsion of the nail, before it is completely separated from the nail bed by pus will probably result in gangrene. Local anaesthesia must never be used It is a safer rule that no operation, apart from amputation, be done on severely ischaemic digits which cannot be performed painlessly without the use of an anaesthetic. A toenail which is raised from its bed by pus can be perforated by a trephine in a number of places, and the trephine holes joined by nail clippers until a large section of the central part of the nail is lifted out Often it is found that the nail is loose, especially that side of it adjacent to the paronychial infection, and it is generally possible to remove half the nail in this way. The relief obtained by decompression is instantaneous, and the toe will generally heal because if there is a sufficient blood supply to form pus, healing is possible. Similarly pus beneath a leathery slough must be released by cutting away the dead tissue, a painless procedure.

from atheromatous plaques higher in the limb. They should be allowed to separate by natural means, the usual care being taken of the feet during the process We have never seen a patient with this uncommon type of gangrene who has demanded active surgical intervention.

Digital gangrene.—Gangrene of the three middle toes, if limited to these can usually be amputated locally through or just proximal to the line of demarcation. If however gangrene involves the dorsum of the foot, a high amputation is usually necessary. Gangrene involving the distal phalanx may not infrequently be limited to the skin, and removal of this dead skin may be all that is required for healing to occur. Involvement of an interphalangeal joint requires at least amputation of the digit, and sepsis of a metacarpo-phangeal joint demands a major amputation.

Gangrene of the little toe generally, but not always, demands a major amputation When it is limited to the distal phalanx local amputation will probably be successful, but when it involves the proximal phalanx, local amputation leaves a wound deficient in skin on its outer side, and therefore one which may not heal. Gangrene of the great toe may similarly be not amenable to local amputation when it spreads over the proximal phalanx, but whether to perform a major or a minor amputation can often be decided with the help of an arteriogram

Amputation of digits or parts of digits is done by the guillotine method, with no attempt at making flaps, as this would result in division of some of the few remaining patent vessels The line of section is just proximal to the line of demarcation. The proximal phalanx is removed by nibbling forceps up to the next joint, and the wound is left open and allowed to heal by secondary intention

Gangrene of the leg.—Massive gangrene of the leg depends on a sudden thrombosis of main vessels in the limb, and is often precipitated by an illness, injury or operation; a major amputation is necessary.

Site of major amputation.—In atherosclerosis there is no place for amputation through the foot or ankle. Although the stump may occasionally heal, it is liable to trophic change and ulcer formation, and has in our experience never been satisfactory.

Above-knee amputation should be avoided Below-knee and especially through-knee amputations are almost always successful [illegible]
suffered above-knee [illegible]
aga [illegible]
nec[illegible]
[illegible] circumstances is beyond them. Rec[illegible] there has been a trend of opinion, based on experience, in favour of below-knee amputation, even in patients with absent femoral pulses, and with extensive gangrene of the foot, and if done with the utmost care to avoid injury to skin flaps it is often surprisingly successful with healing of the stump. If collateral vessels are palpable over the condyles of the femur, or if the

Fig. 240



Fig. 241

result from trauma, often from pressure or locally applied heat (Fig. 243). The dead tissue forms a hard leathery slough of variable thickness, and this slowly separates. The tissues beneath this are the site of an inflammatory reaction, and if infected may give rise to swelling and pain, but pain of ischaemic origin is variable. Unless the slough is deep and involves tendons or underlying bones or joints, local removal will generally leave tissues capable



Fig. 243
Burns from a hot water bottle in a foot already ischaemic.

of repair. The slough can be cut away as it separates and any tension beneath is thereby relieved. Softening of the dead tissue by moist dressings and soaks of the part in half strength eusol solution make removal easier.

When infection is prominent and ischaemia is severe a dirty sloughing ulcer may appear, often on the dorsum of the foot, and if this does not rapidly react to treatment by antibiotics, then a major amputation is necessary.

Treatment of gangrene in association with diabetes.

Atherosclerotic gangrene occurring in a diabetic demands no special treatment apart from that described above with, of course, control of the diabetes.

Infective diabetic gangrene results from sepsis spreading to one or more metatarsophalangeal joints and thence subperiosteally upwards along and around the shafts of the metatarsals. All the layers of the foot are infiltrated by foul pus, often laden with gas forming organisms, and the whole foot is swollen, crepitant and painless, and generally discharging from one or more sinuses, often over metatarsophalangeal joints. In this type of case drainage must be established. In the foot the metatarsals relative to the infected joints must be excised, and this must be done through an incision

popliteal pulse is palpable—very rare in atherosclerosis—then a *formal flap amputation* should be done (p. 799), but in severe degrees of ischaemia a *circular incision, with no suture technique* is preferable[19] (p. 800). Healing, although delayed, occurs, and the patient is left with a stump which can be fitted usefully with a prosthesis. In one clinic[78] 196 *below-knee amputations* were done, the flaps being stitched, with a reamputation rate of 4·7 per cent. Even more successful results may be expected when a circular incision without suture is used.[18]

Below-knee amputation should not be done when there is a flexion contracture of the knee joint, extensive gangrene or infection of the leg, or a recent massive thrombosis of the femoral artery.

Above the knee amputation at the classical site is indicated when there is gangrene involving the upper third of the tibia, and in those patients with iliac or aortic obstruction who suffer a further massive thrombosis of the main vessels of the limb. Certain elderly and bed ridden patients with severe intercurrent disease who by virtue of their general condition will not be able to walk again may be better served by above-knee amputation which will heal by first intention, but it should not be done on both sides.


FIG. 242
Stokes-Gritti amputation A good end bearing stump

There are many advantages in amputation of the Stokes-Gritti type through the condyles of the femur. It usually heals well owing to the richness of the subcutaneous collateral circulation around the knee joint It provides a stump which can be fitted within eight weeks with a serviceable pylon, allowing the patient to get about, and a low " knee-joint " can be constructed to *enable the limb to be bent, although few* amputees accomplish walking with the joint in action and the majority only maintain stability with it locked. A further advantage of this type of *amputation is that if an above-knee* amputation has to be performed on the other limb, the patient is in some measure able to move about and turn over in bed. *A patient with two above-knee amputations* is very helpless, even in bed (Fig 242).

During and after all operations, especially amputations, the greatest care of the remaining heel must be exercised On the operating table during the amputation the unaffected heel must be protected from pressure by suitably placed foam rubber cushions. The *thigh and leg of the remaining limb* can be supported by slings suspended from a beam over the bed, so that no pressure can be exerted on the heel.[18]

Gangrenous ulcers.—These are situated over the outer aspect of the lower part of the leg, over the dorsum of the foot, and particularly over the heel, and

metatarsophalangeal joints is present, treatment on the lines suggested for infective diabetic gangrene should be carried out. We have recently seen a diabetic patient aged sixty-four with absent pulses at the ankle joint, but also with septic arthritis of a metatarsophalangeal joint and gas forming organisms in the pus. The colour of the limb was normal. Removal of the metatarsals and their phalanges was done via an incision in the sole, and the wound eventually healed (Fig. 244). On the day before his planned discharge from hospital he sat with his feet in front of the ward fire, as a result of which they were burned in numerous places (Fig. 244B). Six weeks later these burns were healed.

P. M.

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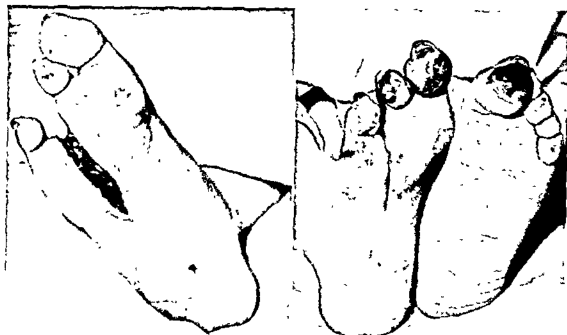
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into the sole of the foot which must extend *sufficiently* far so that with the foot in the position assumed when the patient lies in bed, pocketing of pus cannot occur (Fig. 435). With removal of the metatarsals must be removed the digits which they bear. The wound is loosely packed with Bradosol—*streptomycin locally* is also valuable—and healing takes place rapidly, leaving a deformed but a useful foot and one free from pain owing to the associated neuropathy. Major amputation should never be necessary as the blood supply is not impaired.



A FIG. 244 B

A—The third and fourth metatarsals were removed with their phalanges, on account of infective diabetic gangrene

B—The same patient, who immediately prior to discharge from hospital suffered further superficial gangrene of the toes after sitting in front of an electric fire without his socks and shoes

NEUROPATHIC GANGRENE OF DIGITS.—The blood supply is good, and gangrene is the result of trauma, often burns. In appearance it is similar to that occurring in atherosclerosis, but diagnosis can be made by evidence of neuropathy—diminution or loss of sensation, absent reflexes, and loss of vibration sense, and by the presence of pulses at the ankle joint. Treatment of this type of gangrene is conservative, and amputation is never necessary.

MIXED NEUROPATHIC AND ATHEROSCLEROTIC GANGRENE.—Gangrene due to this double cause may be difficult to diagnose unless evidence of neuropathy is obtained. Ischaemic pain does not occur, but colour changes of persistent rubor or pallor will indicate ischaemia to be the important factor. Where there is doubt conservative treatment should be tried first, and if sepsis of

CHAPTER X

THE PATHOLOGY OF BUERGER'S DISEASE OR THROMBOANGIITIS OBLITERANS

GENERAL CONSIDERATIONS

THE changes in this disease suggest a specific alteration in the blood vessels as its basic cause. *Something occurs which sets up thrombosis in vessels in full physiological activity,* in contrast to those senile or pre-senile vessels in which thrombosis occurs in atherosclerosis. Following upon thrombosis there follow all the changes of active recanalisation in a very striking degree. The affection attacks especially, and in its early stages almost exclusively, the vessels of the lower extremity;[3] including the main vessels of supply, their primary branches, and their finer communications, down to the digital vessels.[4] In its later stages the same changes may be found in the vessels of the arm and hand. It affects the neural and peri-vascular vessels, but is less obvious in those within the muscles. *No pre-existing lesions which may be regarded as the cause of thrombosis are constantly found in the walls of the vessels,* and the question may be asked: Which come first, the vascular changes or the thrombosis? And if the latter, as is generally accepted, may not the cause be a blood dyscrasia rather than a vascular disease? This alternative would seem to be remote, since in blood dyscrasias leading to thrombosis, such as thrombocythaemia, paroxysmal nocturnal haemoglobinuria,[1] leukaemia, polycythaemia,[2] carcinoma of the pancreas,[3] etc., the thrombosis is essentially venous and has a *different distribution*; in that in these conditions it affects especially the larger veins, such as the femoral or iliac, and the visceral and cerebral veins and arteries. Moreover, no evidence of any such blood disorder has ever been [illegible] ; been claimed from time to [illegible] when it is present, may well [illegible]

Superficial phlebitis.—We have said that no pre-existing lesions are found in the vessels to give anatomical evidence of a primary vascular change, but this is not wholly true and the superficial migrating thrombophlebitis of Buerger's disease may be cited against us. This phenomenon occurs in some 40 per cent. of cases of the clinical disease. The pathologist, however, has much fewer opportunities of examining the vessels than this incidence suggests. The venous changes were emphasised by Buerger in his original monograph and illustrated therein as an acute inflammatory condition of the vessel's wall, sometimes resulting in foci of the most acute cellular infiltration, which he called "purulent foci". We have from time to time seen such a picture of acute recurrent phlebitis in superficial veins which have been excised for

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FIG. 245

and B—Thrombophlebitis migrans in the long saphenous vein (below knee) of a male aged 18 Twelve weeks' duration Acute phase with polymorphs and giant cells C—The same vein just distal to the above lesions D—Long saphenous vein of a female aged 32 "Phlebodynia" (*see* p 600) all ×26

painful thrombosis where a diagnosis of Buerger's disease has been made Figure 245 illustrates such veins and shows two sections (A and B) in which the wall is the seat of an acute inflammatory process, without any evidence of local sepsis and with a recent thrombus. At a short distance away from such a lesion the vein may be found markedly contracted and thickened, to an extent which seems certainly pathological (Fig. 245C). We are not altogether satisfied that pictures of this sort are really specific, since they may be given by any localised acute non-suppurative phlebitis. A third condition (D) is also illustrated: this shows an unthrombosed vein which was excised from a female patient, not clinically suffering from Buerger's disease, who complained of persistent pain along the internal saphenous vein and swelling of the limb, a condition which has been called "phlebodynia" (*vide* p. 660). It is noteworthy for the appearance of extreme musculo-elastic thickening of the vessel's coats, which also extended to its valves, and which may well be regarded as pathological; this appearance is not unlike that seen in one of the veins in Buerger's disease (C) beyond the focus of acute inflammation and thrombosis. As a result of experimental observations on limbs in which the vessels have been distended with formalin, we think that this is largely a condition of spasm and not an organic change in the vessels. Whether our interpretation be correct or not, the appearance of such thickened and spastic veins is so common in the deep veins in cases of unequivocal Buerger's disease that it may be considered a usual feature.

The question may also be asked, whether the intense cellular reaction just illustrated in the veins in migrating thrombophlebitis is primary and evidence of disease in the vessel wall, or is it a result of the thrombosis? In the case shown (Fig. 245) it was limited to the thrombosed area and absent from the vein on either side of this. Moreover, the inflammatory change may be restricted to a part only of the circumference of an affected vessel, leaving the rest comparatively healthy From this evidence, and from the fact that venous thrombosis in other sites and in other conditions does not seem to produce anything like the same degree of reaction, we may conclude that the inflammatory changes in the veins in Buerger's disease are more than a general response to the presence of a thrombus.

Morbid anatomy.—A characteristic feature of thromboangiitis obliterans is that it affects both arteries and veins: another point of difference from atherosclerosis. In rather more than half of the cases in which we have examined in a comprehensive fashion the deep and superficial arteries and veins, in a limb amputated for the disease, these vessels appear to be about equally affected; in most of the remainder the arterial changes were the more pronounced. Only exceptionally did the venous changes predominate. Further, in Buerger's disease there is no sparing of the smaller vessels, such as those of the extremities, which is so notable in atherosclerosis (p 340) Whether the lesions in thromboangiitis really commence in the distal vessels, or whether early symptoms referable to the extremities are merely evidence

recanalisation and the transformation of a single lumen into a number of small more or less parallel channels (Fig. 246).

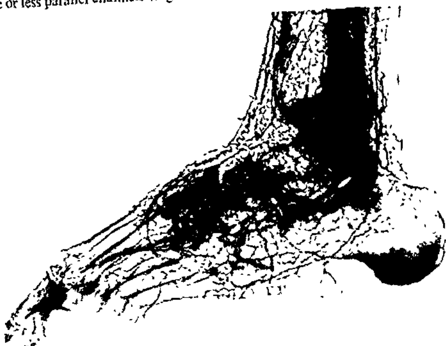


FIG 246
Radiogram of foot (after amputation) in Buerger's disease (Case W.121)



FIG 247
Radiogram of finger Arrow shows apparently normal digital artery from which next figure was taken (Case W 75)

This may be so effective that a vessel may sometimes appear intact in a radiogram and yet on histological examination be found to have been altered by disease. The following case illustrates this:—

Case W. 75.—Symptoms of thromboangiitis for eight years. Left leg amputated three years earlier. Symptoms in hand for four months, with ulceration. Amputation right fourth finger. The radiogram of this (Fig. 247) shows a general distortion of the arterial pattern, but with the preservation of a single digital artery of normal appearance Section of this (Fig. 248) shows, however, that the vessel has in fact been thrombosed and subsequently recanalised, leaving a double lumen

In many post-mortem radiograms the smaller vessels are profoundly altered so that the classical vascular pattern cannot be detected at all, a network of vessels having an unfamiliar arrangement replacing this (Fig. 249). There is again a marked contrast with atherosclerosis (*cf* Fig 205, p 346)

of disease in the more proximal vessels, as in atherosclerosis, it is hard to say. Clinically obstruction of a major vessel, *e.g.* the popliteal, may antedate apparent distal disease by some years but our impression, based on pathological material, is that both are involved together; since whenever we have had an opportunity of examining the proximal and peripheral vessels in one and the same case we have usually found serious involvement in both. It sometimes happens, however, that the severity of the disease seems greater in the larger vessels. This is illustrated by the following case:—

Case W.107: Male, age 28.—The man's left leg had been amputated eighteen months previously. The right leg was now amputated below the knee for increasing pain at rest. There was marked rubor in the dependent position and hyperaesthesia to light touch over a "sock area." No gangrene. Pre-operative arteriograms showed no patent vessel beyond the upper end of the superficial femoral, suggesting very advanced thromboangiitis obliterans. Post-operative arteriograms were not done.

On dissection and histological examination the condition of the vessels was as follows:—

	Anterior tibial.	*Posterior tibial.*	*Peroneal.*
Amputation level.	Lumen reduced to about 1/3 by symmetrical endarteritis.	Obliterated.	—
Mid-leg.	Lumen slightly reduced by ditto.	Obliterated.	Obliterated.
Ankle.	Normal.	Obliterated.	—

Both *plantar arteries* were normal.

The following *digital vessels* were examined:—

4/digit . . The tissues were oedematous and infiltrated with leucocytes and the veins thickened and showed acute thromboses. The arteries were not noticeably affected

3/Digit . Normal

1/Digit . Only moderate chronic arteriolar and venous changes.

The escape of the plantar vessels, the dorsalis pedis, and the minor changes in the digital vessels seen in this case are unusual in our experience.

The effect of the customary widespread disease of the vessels upon the arterial pattern, as seen in post-mortem arteriograms, is profound. Injection is always technically difficult, for the reason that thrombosis and recanalisation have as a rule so altered the vessels that a usable lumen is difficult to find in amputation specimens. The main lines of the main vessels in such a radiogram are often recognisable, but they are apt to appear thin and tenuous from

Histology.—The arteries in thromboangiitis present pictures of active [illegible] which may be found [illegible] sation which we have [illegible] already discussed at length (p. 359), is really the same in either case, and is part of the normal reaction to thrombosis, but in Buerger's disease it proceeds with much more vigour in vessels free from the degenerative changes of advanced life and progressive atheroma; which produce a hardened, rigid and narrowed vessel, with masses of avascular fibrous tissues in its walls, and often with



Fig. 250
Diagram of stages in the recanalisation of an occluding arterial thrombus

the superadded complication of intimal calcification. In thromboangiitis, on the other hand, we have young arteries, fully patent and in full physiological activity, with a healthy wall and a richly cellular intimal coat. In these circumstances the picture develops of a cellular and vascular tissue, derived from the vessel's endothelium and the tissues lying within the internal elastic lamina, filling the lumen and invading and replacing the thrombus. It is also probable that some cells derived from the circulating blood play a part in the recanalisation by developing into endothelium, though this is often denied. All trace of thrombus may be removed as the process advances, except that there are often some residual granules of iron pigment in the cellular tissue. A vascular spongework, with an abundance of through channels, is substituted for the thrombus, and no evidence is seen in the vessel of those degenerative changes which characterise atherosclerosis. The evolution of the process is shown diagrammatically in Figure 250.

The relationship of the vasa vasorum to the process of canalisation is often, we think, misunderstood. In the affected vessels there is a high degree of reaction and dilatation of these small intrinsic vessels, which can only be appreciated well in injected specimens, since the vasa are collapsed in the ordinary histological preparation. It is a striking fact that they appear, nevertheless, to be limited in their inward penetration of the vessel wall by the internal elastic lamina (Fig. 251). This structure, when intact, seems to offer an impenetrable barrier, and though the vasa form a network of great capacity and complexity in the outer and middle coats of the artery, they do not contribute to the recanalisation of the thrombus.

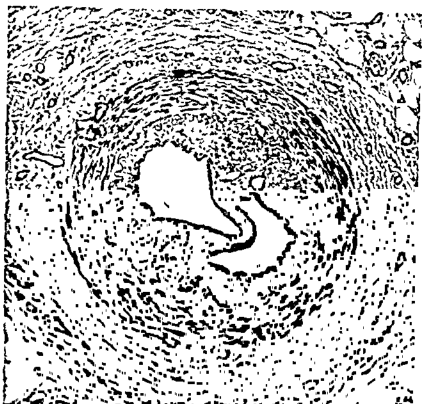


FIG. 248
Section of the digital artery marked in Figure 247 showing double lumen



FIG. 249
Portion of a post-mortem radiogram of the foot in Buerger's disease showing the distortion of the arterial pattern (Case W 104)

Histology.—The arteries in thromboangiitis present pictures of active recanalisation which are far more striking than are those which may be found in atherosclerosis. We believe that the process of canalisation which we have already discussed at length (p. 359), is really the same in either case, and is part of the normal reaction to thrombosis, but in Buerger's disease it proceeds with much more vigour in vessels free from the degenerative changes of advanced life and progressive atheroma; which produce a hardened, rigid and narrowed vessel, with masses of avascular fibrous tissues in its walls, and often with



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Their increased activity in a thrombosed vessel we look upon as a compensatory reaction, to supply nourishment to the deeper layers of the media now cut off by the thrombus from normal imbibition In the veins, which have less well-defined coats, this limitation in extent of *the vasa vasorum is not so marked* .



FIG. 251
Recanalised posterior tibial artery in Buerger's disease, showing the vasa vasorum system of vessels in the muscle and the vertical system of new through channels, separated by the internal elastic lamina Male aged 28 × 60

Though in the view here expressed the vasa vasorum have no part in the extensive recanalisation which goes on, we believe that they contribute to the establishment of a collateral circulation through their plexuses in the adventitial coat, which link one artery to another, and their enlargement *contributes to that inflamed appearance of the neuro-vascular* bundles in Buerger's disease which is so stressed in the literature.

The late outcome of the canalisation process varies a good deal and the *factors determining this are not fully known* In general, it may be said that in the advanced disease the evidence of recent thrombosis and reaction

diminishes and there is a progressive tendency towards *greater* and greater degrees of obstruction to develop in the recanalised vessels, and for the obliteration to become more complete. The vessels also appear to shrink (*see* Figs 252 *to* 254). This complete obliteration is more seen in the smaller (*e g.* the digital) arteries than in the larger limb vessels At times a great excess of elastic tissue forms in and around such occluded or partially occluded vessels; a picture which may not appear in the corresponding vessels in *another* case: this too seems to be correlated with the age of the lesion.

Detailed histology.—There is so much variation from case to case, depending upon the stage of the disease and the characteristic capriciousness of the lesions, that it is difficult to give a single succinct account of the histology of the disease. That it goes through various stages, tending in general from an acute thrombosis, through canalisation, to a final quiescent fibrotic condition of the vessels, with a limited circulation through their recanalised trunks, is beyond doubt; but it is also true that these stages do not coincide in point of time in the different vessels in any one case. Thus, in a limb which shows the quiescent stage in a majority of its arteries it is not unusual to find a recent thrombus in one of them. Further, the histological picture is varied according to the size of the artery and its histological structure. For example, the lesions characteristic of the arteries of the leg are uncommon in the popliteal and larger vessels, whilst the excessive elastosis sometimes seen (Fig. 255) is especially characteristic of the digital vessels and, as we have said, seems to be a feature of long-standing obliteration

With the above provisos we propose to illustrate the histology by describing the findings in a single case, in the same way as we have done with atherosclerosis, and to comment upon their general applicability as the occasion arises.

Case W.112 Male (Polish) age 28.—Amputation of left leg. This man was first admitted to hospital on account of attacks of pain and "pins and needles" in his *right* foot with a well demarcated area of dry gangrene on the distal third of the second toe The femoral [illegible] osterior [illegible] er. An [illegible] tibial.

Right lumber sympathectomy was carried out three weeks later and the second *toe amputated* Following operation the foot became warmer and less painful. He complained, however, of pain in the third toe *on the left side and left* lumbar sympathectomy was carried out about a month after the first operation Six weeks later the right second toe had *not healed: there* was marked rubor on letting the foot hang down A month later he complained of severe pain in his *left* toes and a patch of gangrene had developed *on the right* big toe. An arteriogram now showed deficient circulation in both legs. A left below-knee amputation was done seven months after his initial *admission It* healed well. Five weeks later it was found necessary to amputate *the third toe* of the remaining foot; this healed well. At present the arteries of the right foot cannot be palpated; the foot is cold and on raising and lowering the leg the return of colour is very slow.

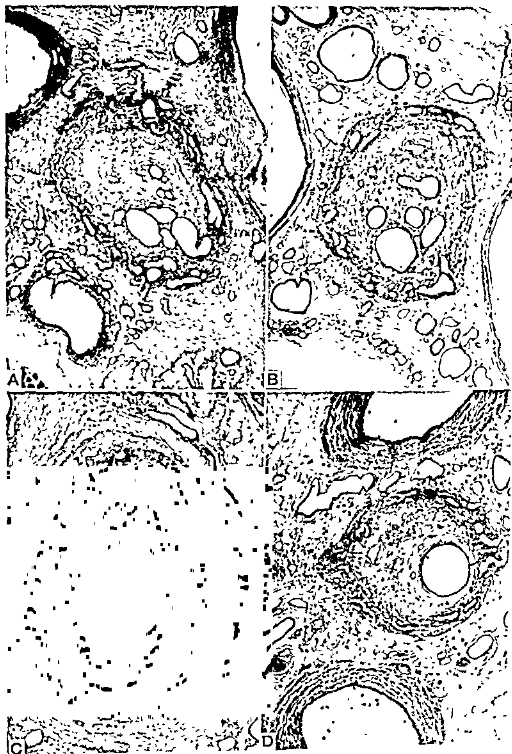


FIG. 252
A and B—Anterior tibial artery at different levels C—Dorsalis pedis artery D—Posterior tibial artery at amputation level All × 30

The histological description which follows is of the vessels in the amputated left leg; in surveying them it is important to note that this limb was perfused with formalin shortly after amputation, and on this account the *vasa vasorum*, veins, and small vessels (in fact all discernible vessels), are unusually prominent. The conditions in the arteries were as follows:—

1. ANTERIOR TIBIAL
   (a) *At the site of amputation.*—The artery is obliterated and shows moderate recanalisation with great development of the vasa vasorum. The large veins and anterior tibial nerve appear normal. A small *arteria comes* shows marked endarteritis obliterans. The neurovascular bundle is excessively vascular. (Fig. 252A) × 30.
   (b) *At mid-leg.*—The arterial lesions are as above. The veins are normal. (Fig. 252B) × 30.
   (c) *Dorsalis pedis.*—The vessel has been obliterated, but is extensively recanalised. (Fig. 252C) × 30

2. POSTERIOR TIBIAL
   (a) *Just below amputation*.—Obliterated and partially re-canalised. Some venous thickening. (Fig. 252D) × 30.
   (b) *At junction of lower and middle thirds.*—As above; but the artery is less well canalised. The veins are normal. (Fig. 253A) × 30
   (c) *At ankle.*—Extensively recanalised The veins are normal and highly patent. (Fig 253B) × 30

3. PERONEAL
   (a) *Just below amputation.*—A healthy dilated vessel. The veins are normal. (Fig. 253C) × 30
   (b) *At junction of lower and middle thirds*.—A normal dilated artery and veins Some foci or cellular infiltration were seen in the perivascular tissues (Fig. 253D) × 30.

4. EXTERNAL PLANTAR ARTERY
   The vessel is patent There is some perivascular cellular infiltration and fibrous thickening (Not figured)

5. INTERNAL PLANTAR ARTERY
   Extensively recanalised. There is periarterial infiltration (Fig. 254A) × 30.

6. DIGITAL VESSELS
   (a) *Fourth digit.*—One digital artery shows old canalised thrombus (Fig. 254B) × 90, the other was patent. Some veins showed recanalisation
   (b) *Third digit.*—One digital artery shows recent organising thrombus (Fig 254C) × 90 The other an old canalised lesion (Fig. 254D) × 90.



FIG. 253
A and B—Posterior tibial artery at different levels. C and D—Peroneal artery at different levels
All ×30



FIG 254

—Internal plantar artery, with branch ×30 B—Digital artery of the fourth toe ×90
—One digital artery of the third toe ×90 D—Another digital artery of the third toe ×90.

The case illustrated may be regarded as showing clinically a rapidly advancing lesion, which on the pathological side is related to a main incidence of the disease in the large arteries of the leg. The changes are histologically of a rather quiescent type and there is little in the way of cellular infiltration or other evidence of inflammatory change. The digital vessels do not show the amount of involvement which is usual where the disease has a slower clinical course. The involvement of the digital veins is likewise much less marked than is often the case. Two other special points of interest are apparent in these sections. Firstly, the large size and relatively thin wall of the patent peroneal artery, the lumen of which is obviously greater than the total cross section of any of the other arteries. Secondly, the largest of the affected arteries (all being shown at the same magnification except the digitals) is the dorsalis pedis. This suggests that this vessel was involved later than either of the tibial arteries, and that it may for some time have received the larger moiety of the blood to the foot, via its anastomoses with the peroneal vessel. Similarly, of the two arteries of the third digit, the one showing a recent thrombosis is much larger than its companion vessel which has an old recanalised lumen.

In other respects the pathological changes, with their lack of degenerative characters and the outstanding evidence of recanalisation are typical of thromboangiitis obliterans.

SPECIAL PATHOLOGICAL EFFECTS IN THE EXTREMITIES IN ATHEROSCLEROSIS OR THROMBOANGIITIS OBLITERANS

In all cases of thromboangiitis obliterans we have examined pronounced disease of the small peripheral vessels, such as the plantars and digitals, can be found, and is indeed a characteristic feature of the condition (Fig. 255); so that the pathologist has little or no difficulty in distinguishing ischaemia in these areas due to thromboangiitis from that due to atherosclerosis. A constant feature in vessels of this order in thromboangiitis is the involvement of both arteries and veins Evidence is found of old and recent thrombosis, the former with canalisation (Figs. 254B, C, D and 255A); of inflammatory lesions in the walls of veins (Fig. 255B); and of old fibrosed and totally occluded vessels Old and recent lesions may be found side by side. In some cases of Buerger's disease there is a pronounced overgrowth of elastic tissue about the occluded vessels: this is by no means always so and when it is found we think it denotes great chronicity in the lesion (Fig. 255B) These lesions differ quite distinctly from those found in atherosclerosis, in which such vessels may show endarterial thickening and an increase in the layers of collagenous tissue within the internal elastic lamina, and also, in the larger ones, some degree of calcification. But in atherosclerosis the veins are usually unaffected and the small arteries, on the whole, remarkably patent. Thrombosis may



FIG 255

occur in such vessels, but is much rarer than in Buerger's disease and when it heals, and is undergoing recanalisation, the whole process has a much more bland appearance and is without the peripheral fibrosis and perivascular lymphocyte collections so often seen in Buerger's disease.

The soft tissues of the digits do not seem to show any specific or characteristic changes apart from those of ischaemia, and their severity depends upon the degree of this. In the advanced stages of Buerger's disease the digits

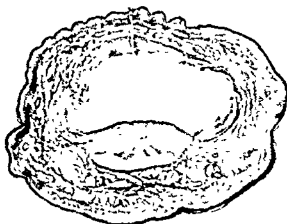


FIG. 256
Ring section big toe at level of distal phalanx in Buerger's disease, showing general dermal fibrosis and loss of fat, with obliteration of vessels (Case W 99) ×2.

often show a notable fibrous thickening of the dermis with some corresponding loss of fat (Fig. 256). These changes are not found in atherosclerosis. The explanation of this difference no doubt lies in the special severity of the lesions in the small distal vessels in Buerger's disease and their freedom from such changes in typical atherosclerosis. The presence of oedema, frank inflammatory change associated with breakdown of the epithelium, and the appearance of infection modify the general picture. We have also noted at times a loss of elastic tissue in the dermis of the digits, but it is not easy to correlate this change with any special variety of chronic ischaemia, or to separate it from the effects of senility.

Nerves.—It is commonly held that there is a specific peripheral neuritis in diabetes and that atrophic changes from this cause are to be found in the nerves of the extremities. The whole question of the effects of chronic ischaemia, diabetes, and senility requires much further investigation and separation. Dr. Duncan Taylor, working in the writer's laboratory, and including in her (as yet unpublished) survey much of this material, has found a regular relationship between the fibrosis of the digital nerve bundles, with associated loss of neurofibrils, and advancing age. This correlation does not

seem to depend upon detectable arterial ischaemia. For such reasons conclusions based upon the casual observation of occasional cases cannot be accepted as *reliable*. With this proviso, it may be said that advanced examples of nerve atrophy are often seen in the digits of limbs which are the seat of atherosclerotic ischaemia, up to the complete disappearance of nerve fibres from certain of the nerve bundles (Fig 257) In about a half of our cases we have



FIG. 257
Extreme fibrosis loss of axis cylinders in a digital nerve (Case W 111) Senile non-diabetic gangrene in a man aged 84. ×90



FIG. 258
Thinned epithelium in atherosclerosis, showing some detachment of the horny layer with atrophic epithelium below. Note large patent artery with a little medial calcification (Case W. 113). ×7.

found well marked changes of this type and in less than a quarter no changes. The incidence of the severest lesions is greatest amongst the diabetic subjects, but they are not confined to diabetics. The lesion is most marked in the nerves of the digits and is not so marked in the larger trunks, such as the posterior tibial or plantar bundles. The changes are to some extent capricious, so that the two main nerve trunks in a single digit may be affected to very different degrees There would seem to be room here for some research into the extent to which sensation suffers in such digits and of a possible correlation with pain.

In Buerger's disease, on the other hand, the nerves of the digits are much less affected and in the majority of our cases showed no changes. It has to be remembered, however, that these patients were as a rule some decades younger than those suffering from atherosclerotic ischaemia. It may be added that we have found no evidence of special nerve atrophy in relationship to areas of acute ulceration and gangrene, and no support for any "trophic" theory of the cause of such lesions.

With regard to the epithelium of the digits, which in the clinical descriptions is often noted to be thin and glazed, we have sometimes found a degree

of atrophy especially on the dorsal surface: the epithelium is thinned and often there is a loose layer of thin keratin overlying it (Fig. 258). This seems undoubtedly to be correlated with the loss of axis cylinders in the peripheral nerves, especially in atherosclerosis, as in the example figured.

THE EFFECTS OF ISCHAEMIA ON OTHER TISSUES

There appears to be nothing specific in the necrotic and gangrenous lesions which affect the extremities in either form of arterial ischaemia. These are associated with infection which brings in its train the customary acute



FIG 259
Chronic ischaemic atrophy of muscle due to obstruction of the posterior tibial artery in Buerger's disease (Case W 30) ×60

inflammatory reaction; the extension of this to such vessels as still are patent may aggravate the condition by the superimposition of acute phlebitis or arteritis, with consequent acute thrombosis. Such late and limited thrombotic lesions are often seen at the edges of an advancing focus of gangrene and are in no way specific.

With regard to muscle: a certain amount of ischaemic muscular atrophy is not uncommon and this, in general, seems produced rather by arterial obstruction before the vessels enter the muscle than by actual lesions of the intramuscular branches In only a few cases we have found marked anatomical evidence of muscular atrophy. There appears to be nothing specific about this, the degree and site being determined by the degree of the arterial obliteration and its anatomical relationship to the supply of the

muscles. A highly developed acute focal obliteration is likely to lead to a focus of acute muscular necrosis, followed by a localised fibrous area of the nature of a Volkman's ischaemic contraction, whilst a more general ischaemia from a larger vessel to a general slow muscular atrophy without replacement fibrosis (Fig. 259). The usual wide distribution of the lesions, which has been emphasised in the previous pages, should make clear the reason why it is the latter rather than the former which one encounters in both types of chronic progressive arterial ischaemia.

J. H. D.

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[3] SPROUL, E. E. (1938) *Amer. J. Cancer* 34, 566; JENNINGS and RUSSELL (1948) *Ann Surg Chicago* 56, 187; SMITH and ALBRIGHT (1952) *Ann. intern. Med.* 36, 90; EDWARDS (1949) *N. Zealand med. J.* 26, 1031; OELBAUM, M. H and STRICH, S. J. (1953) *Brit. med J.* 2, 907.

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FIG. 259
Chronic ischaemic atrophy of muscle due to obstruction of the posterior tibial artery in Buerger's disease (Case W 30) × 60.

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type is more common, often with involvement of the digital arteries alone, at least in the first place, though obstruction in the fingers may be followed by disease in the radial or ulnar arteries or both at a subsequent date. Successive episodes of the disease may affect the arterial tree at different levels and sometimes the arteries of a limb are affected at multiple levels from the onset. The distinction between a proximal and a distal type of thromboangiitis is of clinical importance for it affects treatment and prognosis

The relationship of localised arterial thrombosis to thromboangiitis obliterans has afforded considerable discussion. Sometimes a sudden thrombosis of limited extent affects a short segment of an artery, the popliteal for example, and remains localised to that segment for a long period of time without evidence of any extension. Boyd[11] considers that a popliteal thrombosis in a man of twenty or thirty, without other evidence of arterial disease, is traumatic in origin, the thrombosis being due to a shearing stress between that part of the popliteal artery which lies free and mobile in the loose fibro-fatty substance of the popliteal fossa, and the segment immediately below, which, at the level of the knee joint, is firmly held in a compartment of the oblique ligament. He describes the occurrence of popliteal thrombosis after posterior dislocation of the knee joint, the arteriograms of which are indistinguishable from those of popliteal thrombosis as it is seen in young male adults where there has been no such injury. A similar type of arterial fixation at the junction of femoral and popliteal arteries at the opening in adductor magnus might be held responsible for thrombosis here, another common site Boyd maintains that this kind of arterial obstruction is benign and final and he has followed patients for ten years without the occurrence of any further arterial disease. Palma[12] also subscribes to this theory of a traumatic origin for localised arterial thrombosis and describes the later development of peri-arterial fibrosis around the thrombosed vessel; peri-arterial fibrosis might equally well be cited as evidence that the thrombosis was of the kind met with in thromboangiitis obliterans. Telford[8] considers this type of thrombosis results from the lodgment of an embolus originating in an atheromatous plague at a proximal level in the femoral artery. Learmonth *et al.*[13] reported three cases of "localised arterial thrombosis of undetermined origin," and Richards has described a fourth case from the same clinic, but of these four patients two have now developed further arterial and venous thrombosis, and show all the characteristics of Buerger's disease, with its usual episodic course, and one of the patients is untraced.[10]

It therefore seems that a proximal acute arterial thrombosis in a young man can be a manifestation of Buerger's disease, and in fact a not uncommon one, and that a traumatic origin is exceptional Allen Barker and Hines[14] consider that thrombosis in a larger vessel such as the femoral or popliteal is a definite though rare starting point for the disease. Sometimes undoubtedly there may be a massive thrombosis of the popliteal artery and its branches as an acute episode, but more often this is a later stage of the disease following

CHAPTER XI

THE SURGERY OF BUERGER'S DISEASE OR THROMBOANGIITIS OBLITERANS

IN 1879 Von Winiwarter described an inflammatory disease of the arteries and veins of the leg of a male patient. Gangrene developed in the affected limb and amputation had to be performed. Von Winiwarter's description of the clinical course of his patient and the detailed histology of the amputated limb have all the characteristics of what is now known as thromboangiitis obliterans.[1] Before Von Winiwarter's paper this disease had not been distinguished from other cases of arterial obstruction. In 1908 Leo Buerger[2] published eleven similar cases of ischaemia and gangrene of limbs resulting from an inflammatory lesion of the arteries. He called the condition thromboangiitis obliterans, and the disease became established as a specific entity. Later, in 1924, he published a monograph on the subject with detailed clinical observations and a description of the pathological appearances in all stages of the disease, and it was not until this time that the condition was widely recognised as an entity distinct from atherosclerosis. In more recent years several important papers, notably those of Telford and Stopford[3,4] Brown and Allen,[5] Telford,[6] Lynn and Burt,[7] Kinmonth,[8] Campbell *et al.*[9] and Richards[10] have extended knowledge of the disease.

GENERAL CONSIDERATIONS

Thromboangiitis obliterans is an episodic and segmental inflammatory lesion of the arteries and veins, resulting in permanent obliteration of their lumina, occurring predominantly in males between the ages of twenty-five to forty years and involving generally, but not exclusively, the vessels of the limbs. The effects of the disease are almost solely due to obstruction of the arteries, and the symptoms are due in the main to ischaemia, sometimes complicated in the later stages by infection of devitalised tissue The inflammatory process which involves the vessels exhibits phases of activity separated from each other by periods of inactivity which vary greatly in duration; ten years or more may pass without any advance in the disease, or episodes may recur at intervals of a few weeks.

The vessels most commonly first affected are the arteries of the legs, especially the posterior tibial. The peroneal artery seems to be remarkably free from liability to involvement, at least in the early stages of the disease A distal type of thromboangiitis obliterans may affect and obstruct the plantar or palmar and digital arteries, and a proximal variety may affect primarily the popliteal artery or femoro-popliteal trunk. In the upper limb, the distal

demonstrated distally. More usually the changes in nerves result from ischaemia, rather than strangulation, and sometimes the vasa nervorum themselves are *obstructed* by thrombosis with consequent degeneration of nerve fibres. Such pathological changes as occur in other tissues are those of ischaemia. Muscles often atrophy, and in severe cases the atrophied muscle may be replaced by fibrous tissue, skin may become atrophic and thin, the nails may show irregular growth, and subcutaneous fat may disappear. Bone, as the result of persistent ischaemia, may be affected by osteoporosis often accentuated by disuse, and if infection should occur by way of an overlying ulcer osteomyelitis may become established. Joints may be similarly affected by infection admitted through a perforating ulcer, and the metatarso-phalangeal joints are particularly liable to this kind of inflammation. Ulceration or gangrene of the extremities is frequently seen, in a majority of cases being precipitated by thermal, chemical or mechanical injury.

CHANGES IN THE BLOOD

Changes have frequently been described in the blood, but have not been shown to follow any uniform pattern. Haemoconcentration,[17] increase of phospholipids,[18] increased viscosity of the blood[19] and low oxygen content of the arterial blood[19] have all been reported in the disease, but there is little evidence that any of these conditions have more than a chance relationship.

AETIOLOGY

Age and sex incidence.—The disease starts nearly always but not invariably between the ages of twenty and forty years, and although it may first be seen and diagnosed at a later age, the history usually dates back to an age earlier than forty years. In forty-one patients seen by us during the last seven years the age of onset has been from twenty-two to forty-nine years with an average of thirty-four years. Allen *et al.*[14] mentioned a case in which symptoms appeared at the age of seventeen; Telford[6] that of a child of eight; and Horten and Brown[20] a number occurring above the usual age group.

The disease may occur, though very rarely, in women. There have probably been less than ten proven and undoubted examples reported in the literature, and we have seen only one woman in whom the diagnosis can be strongly argued.[21]

A woman, aged thirty-six years, was admitted to hospital with evidence of peripheral vascular disease of the lower limbs At the age of two weeks, four toes of the left foot had been amputated for gangrene. Thereafter the left foot had been pain free, though always blue and cold, until the age of thirty-two years when there had been a rather rapid onset of intermittent claudication in the foot.

On admission to hospital at that time the left calf was wasted, the left foot was cold and cyanosed and the single remaining toe of that foot was ulcerated A left lumbar sympathectomy was performed and the toe amputated The wound of

on a primary popliteal thrombosis or ascending from the more common distal type of disease.

The episodic nature of the disease usually allows the collateral circulation to develop in response to each successive block, and in some cases indeed the disease process appears to become spontaneously arrested, and when that happens the patient may be left subsequently with only the most meagre evidence of ischaemia. On the other hand progress may be rapid with short intermissions, particularly in the younger age group from twenty to thirty years, and then it is not uncommon for one major amputation or more to become necessary within a year or two of the first appearance of the disease. An episode of extension of disease in the arterial trunk may or may not be accompanied by superficial phlebitis, and superficial phlebitis may occur unaccompanied by detectable arterial obstruction.

Although in thromboangiitis obliterans the legs are affected more commonly than the arms, the arms are affected relatively more commonly in this disease than they are in atherosclerosis, and evidence of arterial disease in the hand of a young man, the Raynaud's phenomenon for example or the absence of one of the pulses of the wrist, is very suggestive of thromboangiitis obliterans. Boyd[15] differs from most authors in finding that involvement of the upper limb is relatively more common in atherosclerosis than it is in Buerger's disease; in our experience, atherosclerosis of the vessels of the upper limbs with subsequent thrombosis is distinctly uncommon.

Thromboangiitis obliterans may exceptionally occur in sites other than the limbs. Its occurrence has been recorded in the spermatic and inferior mesenteric arteries,[6] and other authors have seen the aorta, cerebral, coronary,[6] hepatic, splenic, renal, pulmonary and gastric arteries[16] involved. In a series of patients suffering from thromboangiitis obliterans studied by Kinmouth[8] two died from coronary disease, and one from mesenteric thrombosis, though there was no proof that these vessels were the site of this disease Similarly in an analysis of 28 deaths in a series of 149 patients with thromboangiitis. Campbell *et al*[9] found that 75 per cent. of these died as the result of some vascular incident, coronary, cerebral or embolic, but no proof was obtained in any case that the vessels were involved by thromboangiitis. All that can be said is that patients with this disease appear to have a tendency to the development of visceral vascular lesions.

Changes in the Tissues of a Limb affected by Thromboangiitis

In general the effects of this disease on the tissues of an affected limb are those of ischaemia. The only structures other than the arteries and veins which may be directly affected by the disease are the peripheral nerves These, in some cases appear to be involved by the periarterial and perivenous fibrosis associated with the disease, and Wallerian degeneration may be

Eosinophils 2 per cent.; Basophils 1 per cent.; Monocytes 10 per cent.) Cold Agglutination Titre: 8 per cent. at 2-5°C.; nil at 20°C. and 37°C. No evidence of Cryoglobulinaemia; W.R. Negative; Urine: Sugar, albumen and haemoglobin absent; 17-Ketosteroids (Total for twenty-four hours) 6.0 mg.; Creatinine (Total for twenty-four hours) 720 mg; E.C.G. within normal limits

Radiology.—Chest—nothing significant; Limbs—no *arterial calcification.*

Arteriography.—Percutaneous (50 per cent. Pyelosil). Left leg: the dorsalis pedis did not fill and the lower half of the posterior tibial was not outlined, the plantar artery being filled by collaterals. Right leg: the lower half of the anterior tibial and the lower two-thirds of the posterior tibial were not filled. The dorsalis pedis was patent only in its proximal part, and the plantar artery was filled by collaterals. The major vessels of both limbs appeared normal (Fig. 260). A right



FIG 261

Biopsy of dorsalis pedis artery and associated vein ×45 (*British Journal of Surgery.*[21])

lumbar sympathectomy was performed and a biopsy taken of the right dorsalis pedis artery. Convalescene was uneventful and one month later the claudication in the right foot, though relieved, was not cured, and there was some pain in the right calf suggestive of claudication There had also developed a Raynaud phenomenon in three fingers of the left hand.

Pathological report on the excised dorsalis pedis artery (*Prof. C. V. Harrison*).—The lumen of the artery is occluded by fibrous connective tissue containing a few well-formed arterioles and venules and a few lymphocytes and histiocytes. The internal elastic lamina is unbroken and is thrown into deep folds The media is [illegible] It is traversed by numerous enlarged [illegible] fibrosis and contains an excessive [illegible] fibrous thickening surrounding the [illegible] s the scarred stage of a previously active lesion and it is, therefore, not possible to make a dogmatic diagnosis. In my opinion this is the healed stage of thromboangiitis obliterans (Figs. 261 and 262).

At the present time, three years later, there is obliteration of both popliteal arteries, and intermittent claudication in both calves.

the foot healed by first intention and the foot has remained warm since, with no further claudication for two and a half years. Eighteen months later claudication and cyanosis of the right foot developed. There had been no incident of thrombo-



FIG 260
The distal vessels are narrowed and often obstructed The proximal vessels are patent and apparently normal A common appearance in thromboangiitis obliterans

phlebitis On examination she appeared a healthy looking young woman, there was wasting of the left calf but the left foot was warm and dry and the amputation stumps were all soundly healed. The right foot was cold and there was some skin atrophy, with rubor on dependency and pallor on elevation There were no palpable pulses below the popliteal vessels in either leg.

Blood examination.—Haemoglobin 13·5 gm per cent. (91 per cent.); W.B.C. 10,000 per cm., (Polymorphonuclears 72 per cent ; Lymphocytes 15 per cent.;

the aetiological responsibility of smoking in an individual case, it must be remembered that in advanced disease there is often intense pain, anxiety and loss of sleep, all of which tend to increase cigarette smoking; it is often difficult to elicit how heavy a smoker the patient has been at the time of onset of his disease. Silbert[22] maintains he has never seen a typical example of the disease in a non-smoker and Wright[23] agrees with him. There is little doubt that the great majority of sufferers are cigarette smokers, and a study of 150 patients with the disease revealed only three non-smokers, whereas in a control group of patients of the same age and sex, forty were non-smokers. Furthermore, sufferers from thromboangiitis smoked more per head than those in the control series[24] In the eighty-five cases reported by Richards all were smokers, but few could be considered heavy smokers. All our patients have been cigarette smokers, but some have been light smokers, two recently seen by us using less than five cigarettes per day. Non-smokers are unquestionably affected sometimes, as in the case reported by Telford[5] of a patient who lost both legs from typical thromboangiitis obliterans; and who had been in constant training as an athlete, eschewing smoking completely up to the time of the onset of the disease. Kinmonth[8] has also reported undisputed examples of the disease in non-smokers.

It has been claimed that a patient with established disease who gives up smoking may well suffer no further episodes, and there is evidence that this is so. In a study of 120 patients with the disease there was no progress for periods varying from six months to six years in sixteen, fifteen of whom had abandoned the habit[7] The disease certainly progresses sometimes in spite of patients giving up smoking completely, and commonly it may appear to remain quiet in those who refuse to do so.

Reaction to injection of various tobacco extracts has led to conflicting results[25, 26]

At the present time there is insufficient evidence to incriminate tobacco as the chief aetiological factor in the disease yet it seems to have an important contributory significance, and it is wise to prohibit its use in patients who suffer from thromboangiitis obliterans.

Separate from the possible effect of tobacco as an aetiological factor in thromboangiitis obliterans, is the question whether smoking causes peripheral vasoconstriction Oldham and Pemberton[27] found that in a group of 400 patients suffering from the claudication of atherosclerosis, there were only two who were non-smokers, the consumption of tobacco in the remainder being distinctly high Although claudication is a subjective symptom, difficult for the clinician to assess, occasionally a patient who suffers from it will become completely free of pain on exercise if he or she gives up smoking. The pathological effects of the inhalation of tobacco smoke have been widely studied, but the results of these studies are conflicting Temperature changes and plethysmographic evidence of vasoconstriction have been recorded after smoking a single cigarette. Shepherd[28] has reported, and Roth *et al*[29] have

This case is of peculiar interest in that there was a vascular incident at birth resulting in the loss of four toes, and no further incidents until the age of thirty-two years, when the left foot became affected more severely, and a year later the right foot also, with the appearance of a Raynaud's phenomenon in the hand, and three years later further major arterial obstruction in the popliteal vessels. The history and the microscopical findings are both highly suggestive of thromboangiitis obliterans. Whatever the aetiology of the gangrene in infancy, symptoms suggesting thromboangiitis started at the age of thirty-two years at the latest.



FIG. 262
Biopsy of dorsalis pedis artery ×67 5
(*British Journal of Surgery* 21)

This disease then, though its rare occurrence in women is admitted, can for practical purposes be considered to be confined to the male sex. It may be that oestrin protects the individual against the onset or progress of the condition, or alternatively that the presence of the male hormone is necessary for the disease process to become established, but either of these assumptions must be regarded as highly conjectural.

Race incidence.—Buerger and others considered that the disease was almost confined in its incidence to the Jewish race and particularly to Jews from Poland. This racial distribution of the disease is now disproved. It can occur in probably any white race, and has been reported in Chinese, Japanese, Koreans, Siamese and Negroes. Only two of forty-one of our recent patients have been Jews, and Richards in Edinburgh[10] found only one Jew in eighty-five patients, the majority being Scots. Geographical circumstances do not appear to have any aetiological significance, although symptoms may be more marked in cold weather.

Tobacco.—Tobacco and particularly cigarette smoking is considered by many to be of direct aetiological importance in the disease. Before assessing

the aetiological responsibility of smoking in an individual case, it must be remembered that in advanced disease there is often intense pain, anxiety and loss of sleep, all of which tend to increase cigarette smoking; it is often difficult to elicit how heavy a smoker the patient has been at the time of onset of his disease. Silbert[22] maintains he has never seen a typical example of the disease in a non-smoker and Wright[23] agrees with him. There is little doubt that the great majority of sufferers are cigarette smokers, and a study of 150 patients with the disease revealed only three non-smokers, whereas in a control group of patients of the same age and sex, forty were non-smokers. Furthermore, sufferers from thromboangiitis smoked more per head than those in the control series.[24] In the eighty-five cases reported by Richards all were smokers, but few could be considered heavy smokers All our patients have been cigarette smokers, but some have been light smokers, two recently seen by us using less than five cigarettes per day. Non-smokers are unquestionably affected sometimes, as in the case reported by Telford[6] of a patient who lost both legs from typical thromboangiitis obliterans; and who had been in constant training as an athlete, eschewing smoking completely up to the time of the onset of the disease. Kinmonth[9] has also reported undisputed examples of the disease in non-smokers.

It has been claimed that a patient with established disease who gives up smoking may well suffer no further episodes, and there is evidence that this is so. In a study of 120 patients with the disease there was no progress for periods varying from six months to six years in sixteen, fifteen of whom had abandoned the habit.[7] The disease certainly progresses sometimes in spite of patients giving up smoking completely, and commonly it may appear to remain quiet in those who refuse to do so.

Reaction to injection of various tobacco extracts has led to conflicting results [25, 26]

At the present time there is insufficient evidence to incriminate tobacco as the chief aetiological factor in the disease yet it seems to have an important contributory significance, and it is wise to prohibit its use in patients who suffer from thromboangiitis obliterans.

Separate from the possible effect of tobacco as an aetiological factor in [illegible] hether smoking causes peripheral [illegible] found that in a group of 400 [illegible] claudication of atherosclerosis, there were only two who were non-smokers, the consumption of tobacco in the remainder being distinctly high Although claudication is a subjective symptom, difficult for the clinician to assess, occasionally a patient who suffers from it will become completely free of pain on exercise [illegible] The [illegible] studi [illegible] and [illegible] evidence of vasoconstriction have been recorded after smoking a single cigarette. Temperature changes [illegible] Shepherd[28] has reported, and Roth *et al.*[29] have

This case is of peculiar interest in that there was a vascular incident at birth resulting in the loss of four toes, and no further incidents until the age of thirty-two years, when the left foot became affected more severely, and a year later the right foot also, with the appearance of a Raynaud's phenomenon in the hand, and three years later further major arterial obstruction in the popliteal vessels. The history and the microscopical findings are both highly suggestive of thromboangiitis obliterans. Whatever the aetiology of the gangrene in infancy, symptoms suggesting thromboangiitis started at the age of thirty-two years at the latest.



FIG. 262
Biopsy of dorsalis pedis artery ×67 5
(*British Journal of Surgery* 21)

This disease then, though its rare occurrence in women is admitted, can for practical purposes be considered to be confined to the male sex. It may be that oestrin protects the individual against the onset or progress of the condition, or alternatively that the presence of the male hormone is necessary for the disease process to become established, but either of these assumptions must be regarded as highly conjectural.

Race incidence.—Buerger and others considered that the disease was almost confined in its incidence to the Jewish race and particularly to Jews from Poland. This racial distribution of the disease is now disproved. It can occur in probably any white race, and has been reported in Chinese, Japanese, Koreans, Siamese and Negroes. Only two of forty-one of our recent patients have been Jews, and Richards in Edinburgh[10] found only one Jew in eighty-five patients, the majority being Scots. Geographical circumstances do not appear to have any aetiological significance, although symptoms may be more marked in cold weather.

Tobacco.—Tobacco and particularly cigarette smoking is considered by many to be of direct aetiological importance in the disease. Before assessing

considerably less common amongst those who live in their own residences. If dermatophytosis is an important aetological factor, then it would be expected that thromboangiitis would be more frequent especially amongst those who are specially exposed to the infection This has not been the case in our experience.

In no case of established thromboangiitis has the fungus been detected in the vascular lesion. It might be that some patients are sensitive to a toxin elaborated by, or through the action of the fungus, but why such few patients should be so sensitive, and the vast majority not, would be difficult to explain

Fungus infection when present may well lead to secondary infection of devitalised tissues, and as such should be prevented or treated.

Psychosomatic factors.—Psychosomatic factors are considered by some to be of importance in the aetology of the disease.[9] A sufferer from thromboangitis might well develop anxieties and worries, and it seems more probable that any mental change is resultant on the disease, rather than an aetiological factor

SIGNS AND SYMPTOMS

The clinical features of thromboangiitis obliterans are diverse and vary not only with the site of incidence, but also with the rapidity of the disease process. The majority of the symptoms result from ischaemia, although phlebitis is frequent, occurring either as a first symptom or later in the disease Pain is present in almost all [illegible]
It is [illegible]
ische [illegible]
that [illegible]
Rayi [illegible] digits, or a persistent ulcer may be the first sign of the disease The disease may start with the signs and symptoms of an abrupt major arterial occlusion with the sudden onset of intermittent claudication, pallor, and coldness paraesthesia or numbness, or, where the femoropopliteal artery is involved, by loss of sensation of a sock distribution In these circumstances the severity of the initial symptoms is usually greater in thromboangiitis obliterans than it is in atherosclerosis, as in the latter final obliteration by thrombosis has been preceded by narrowing of the lumen, with consequent development of the collateral circulation, whereas in the former there has been no such preparation by gradual narrowing

Recovery from this acute stage without loss of tissue from necrosis is usual, as the segment of vessel involved is often short, and as the subjects of the disease are generally below the age of forty years the collateral vessels are capable of functioning sufficiently Rarely a massive thrombosis of the popliteal artery and its branches occurs resulting in a major gangrene as a first incident

Involvement of the digital vessels gives rise at first to Raynaud's phenomenon and, later, as the disease advances, to pain, permanent colour

denied, that as great a decrease in flow may be registered after "smoking" an unlighted cigarette as after smoking a lighted one; peripheral vasoconstriction is certainly a normal physiological response to deep inhalation. Mullinos and Shulman[30] found that the smoking of a de-nicotinised cigarette actually caused a greater decrease of blood flow in the hand than the smoking of an ordinary cigarette, and deduced from this that nicotine does not play much part in the vasocontriction of smoking. Smoking at a very rapid rate certainly produces a vasoconstrictor effect which seems to be due to the pharmacological action of some element in the tobacco smoke, as if cigarette smoke is inhaled at about three times the normal rate, the flow of blood in the hand gradually decreases;[28] this rate of smoking is so much beyond normal social habit that the results of this experiment do not seem to be germane to the clinical problem.

The experimental evidence that smoking is vasoconstrictor in its effects is then contradictory, but it does seem sufficient to justify advising against its use in vascular disorders.

Cold and exposure.—Injury, cold and exposure have been blamed for thromboangiitis and admittedly they often precipitate symptoms, but it seems unlikely that they are ever the cause of the disease. We have seen the disease develop five and seven years after frostbite and twenty-five years after immersion foot. The study of a large group of men and women in the fishing industry where exposure is the rule, revealed no case over a period of four years, but significant figures are not available.[31] The incidence of thromboangiitis seems to be less in persons exposed to cold or wet by reason of their profession, than in those who are not so exposed.

Infection.—The inflammatory nature of the pathological process in the vessels has been advanced as evidence of an infective origin, either bacterial or virus in nature[32, 33] and focal sepsis has been considered as a casual factor[3] A possible association between typhus and thromboangiitis has been suggested and it is claimed that rickettsial bodies have been found in vessels the site of the disease.[34] The histological pattern of the changes in the vessels is certainly very suggestive information, but there is no positive evidence of the presence of an actual infecting organism. Cultures from the acute lesion of superficial phlebitis are sterile. Even so, it has never been disproved, and it would be difficult to disprove, that a virus is responsible.

The frequent association of dermatophytosis of the toes with thromboangiitis obliterans has many times been noticed[35] and some consider there is a causal relationship[36, 37] The evidence for this appears to be meagre Although some patients with thromboangiitis obliterans have this infection, by no means all so suffer. Lynn and Burt[7] found that of 120 patients with thromboangiitis, 106 had no evidence of such infection. Dermatophytosis, especially in institutions, such as boarding schools, and in the Services, where communal washing facilities are frequent, is almost universal, though it is

the inflammation resolves to leave a palpable, but painless, nodule of organising thrombus which gradually disappears over the ensuing weeks. Attacks recur at intervals of months or years, and may precede by long periods any clinical evidence of arterial obstruction. One of our patients, a German of Jewish origin, aged twenty-three years, developed superficial thrombophlebitis of a vein of the dorsum of the foot, which resolved without disability. Attacks of



FIG 263
Recurrent superficial thrombophlebitis There were no symptoms of ischaemia, but the inflammatory reaction throughout the vein is typical of thromboangiitis obliterans

superficial thrombophlebitis occurred thereafter at intervals of six months to two years, affecting the arms, legs and abdominal wall Ten years after the first attack biopsy of a recent phlebitis of a vein in the inner side of the left thigh revealed the changes characteristic of thromboangiitis obliterans (p 417) (Fig 263); at this time, no arterial deficiency could be detected in the limbs (Fig 264)

changes, ulceration or gangrene. Intermittent claudication in the foot and calf muscles is very frequent, and occurs rarely in the hand, and coldness of the involved limb is almost invariable at some stage in the disease, and may be a presenting symptom. Paraesthesia of numbness, coldness, heat and tingling frequently occur.

We have found the initial symptoms in forty-two cases have been, in order of frequency:—

1. Intermittent claudication	11
2. Recurring superficial thrombophlebitis	11
3. Persistent ulcer of toe, usually painful	7
4. A Raynaud's phenomenon	4
5. Rest pain in the foot	3
6. Coldness of feet	2
7. Paraesthesiae	1
8. Swelling and cyanosis of toes	1
9. Swelling of leg	1
10. Deep vein thrombosis of a leg	1

Intermittent claudication.—This is the commonest symptom of the disease occurring most frequently in the calf muscles. It may occur at this site either as a result of obstruction of the femoropopliteal artery, or when this vessel is patent, as a result of obstruction of the tibial vessels, which contribute a large blood supply to the deep flexor muscles of the calf. The muscles, rarely of the hand, more often of the foot, are the site of pain on exercise and in the former, writing more than a few words may become impossible. Following acute obstruction of a short segment of vessel claudication may be severe, but provided there is no progression of the disease, this symptom may become less severe as the result of development of collateral vessels and after three to six months it may even disappear. This improvement of exercise tolerance may erroneously be attributed to some therapeutic measure, or to the beneficial effects of the cessation of smoking.

Recurring superficial phlebitis.—Attacks of recurring superficial phlebitis occur in 30 - 40 per cent. of all cases. They differ in some respects from the superficial phlebitis of varicose veins. A shorter length of vein, and often a tributary vein such as that on the dorsum of the foot, hand, or wrist is likely to be affected in Buerger's disease, while in the superficial phlebitis of varicose veins the main trunks of the internal and external saphenous systems are usually involved, though this distinction is not precise In Buerger's disease, while longer segments may be affected, the thrombophlebitis is more often limited to less than an inch or so of the affected vein, and the veins of the upper limb may be inflamed as well as those of the lower limbs. There may be multiple areas of phlebitis scattered over a limb or over more than one limb. Typically a tender red painful swelling appears in the line of a superficial vein, often with slight oedema around it After ten or fifteen days

Raynaud's phenomenon.—When Raynaud's phenomenon in the fingers is the first symptom, it may be difficult to find clinical evidence of organic vascular obstruction, but arteriography and plethysmography will reveal some degree of narrowing or patchy obliteration of the digital vessels and there is failure to achieve maximum flow on reflex heating or nerve block. The suggestion that vasospasm without organic change in the arteries is frequent, appears unproven. After a period of observation of patients with Raynaud's phenomenon, other evidence of the disease such as recurring superficial phlebitis, claudication or absence of a distal pulse appears and the diagnosis of thromboangiitis obliterans is highly probable. Raynaud's phenomenon in the fingers is not symmetrical.



Fig. 265
Persistent ulcer of great toe of a foot from which another toe had been amputated previously for a gangrenous ulcer.

Raynaud's phenomena in the feet tend to affect not the digits only, but the whole forefoot and is often, when prolonged, associated with numbness. Frequently it is induced by exercise, muscle flow being increased at the expense of skin flow.

Rest pain.—Rest pain is considerably more common in thromboangiitis obliterans than it is in atherosclerosis. Obliteration of the terminal vessels of the extremities gives rise to a more severe local ischaemia than is the case when the obstruction is proximal with patent distal vessels (*p. 330*). The pain is in the nature of a deep, gnawing, persistent ache, often worse at nights and interfering with sleep. It is situated in that part of the foot where ischaemia is most severe, and may be localised to a digit or involve the whole foot. The patient grasps and rubs the foot in an endeavour to relieve the pain; he becomes haggard from loss of sleep and a wreck of his former self. Ulceration and sepsis increase the severity of the pain as a result of increase of tension within the tissues. Rest pain varies with ischaemia, and there is no proof that it is the effect of perineural fibrosis.

Pain of a shooting, stabbing, lancinating nature sometimes occurs in thromboangiitis, but is more frequent when the arterial obstruction is proximal, and is therefore seen more often in association with atherosclerosis. It tends to affect the leg and foot and bears no relationship to any particular

Deep vein thrombosis in the lower extremity has occurred only once in our personal series and appears to be rare, though instances of this have been reported by others.[14] In thromboangiitis, since short segments of the veins are affected, it may well be that thrombosis could occur in the deep veins of the lower limb without the development of symptoms, the collateral circulation being adequate to compensate for the loss of a short venous segment. In one



FIG 264
Superficial thrombophlebitis in thromboangiitis obliterans
The phlebitis involves both limbs in patches

of our patients, a Polish Army Officer, aged thirty-four years, the first sign of the disease was phlebitis of the axillary vein. There was sudden pain and swelling in the region of the left shoulder and upper arm, the pain easing after two weeks, but some degree of swelling persisted in the left arm and, to a lesser degree in the forearm. Six years later coldness and paraesthesiae, and eight years later intermittent claudication, developed in the right lower limb and evidence was then obtained of arterial obstruction of both distal and proximal types. There is, however, no direct proof that the axillary vein phlebitis was caused by Buerger's disease

Persistent ulcer of toe.—These ulcers result usually from sepsis arising from unnoticed trauma or as the result of a paronychial infection. Frequenly injury to the toe from ill-fitting footwear can be incriminated. Though sometimes painless at first, local infection and extension of thrombosis, in the adjacent arteries of the digit may result in pain A single toe is often affected, the remaining toes being apparently normal, and there may be no detectable diminution of pulses at the ankle joint. The failure of a paronychia to heal following adequate drainage is very suggestive of arterial insufficiency (Figs 265 to 267).

BURNING AND "PINS AND NEEDLES" are occasional complaints and are often present when the small distal vessels are obstructed. Trophic changes may be present, and the affected area is often hyperaesthetic and frequently ruberose

Swelling of an extremity.—This is an unusual presenting sign but when it occurs is due to deep vein thrombophlebitis, but it is seen not infrequently in the later stages of the disease It may then be due to excessive exudation from stagnating capillaries, persistent dependency, a position assumed to ease rest pain, or rarely to thrombophlebitis of the deep veins of the limb (Fig 268) When an unhealed ulcer or paronychia is present, infection and lymphangitis play their part in the production of oedema Swelling occurring late in the disease is a serious sign implying a threat to the life of the limb.

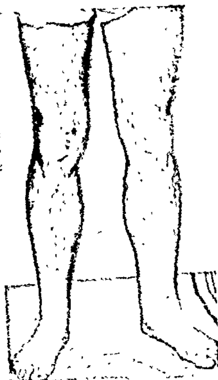


FIG 268

Deep thrombophlebitis occurring as a presenting symptom in a man of thirty-seven years who within six months developed signs and symptoms of arterial ischaemia

LEVEL FIRST AFFECTED

The diagnosis of the early distribution of the disease is based on the history and clinical features of the particular patient and is supported by arteriograms in some Intermittent claudication with colour changes in the foot varying with dependency and elevation, without trophic change distally, together with an impalpable popliteal pulse indicate a femoro-popliteal thrombosis, but it is very probable that some of these patients also have disease of the tibial vessels. A similar clinical picture with a palpable popliteal pulse is taken to indicate primary tibial disease When patients present with a Raynaud phenomenon, painful ulcers, persistent rubor or incipient gangrene of digits with a pulse palpable at the wrist or ankle the disease is considered to be of a distal type.

Of forty-two patients recently seen at Hammersmith Hospital the incidence was proximal at first in 55 per cent , starting apparently in the femoro-popliteal artery in 18 4 per cent and in the tibial vessels in 36 8 per cent , whereas it was distal in 36 8 per cent of patients The hands were involved at some stage of the disease in 34 per cent of cases, and in 13 per cent symptoms were restricted to the upper limbs at the time when the patient first presented

nerve territory. The precise course of the pain is obscure, but it is said to be a symptom of "ischaemic neuritis." This theory appears questionable (p. 424).



FIG. 266
Persistent paronychia of great toe Amputation of the toe was done and section showed changes typical of thromboangiitis obliterans.



FIG. 267
Persistent ulcer of a finger which had been the site of a disabling Raynaud's phenomenon

Coldness of the feet.—This is a common early symptom of the disease and is usually more marked in one limb, in fact it is of little significance if it is not so It may involve the whole or part of the foot, and is often accompanied by numbness and paraesthesiae. It is more common when the disease is proximal, and is not usually associated with pain, or it may be that the intensity of rest pain in thromboangiitis overrides the sensation of coldness.

Paraesthesiae. — NUMBNESS occurs occasionally early in the disease, and is frequently accentuated by exercise, when sensation may become so blunted that there is a feeling of unsteadiness on walking. Like the pain of claudication, it may recover on resting, but if it is associated with loss of sensation of "sock" distribution it is an indication that ischaemia is severe and acute It is often associated with Raynaud's phenomenon affecting the whole forefoot, and is generally relieved following a sympathectomy. It appears therefore to be due to interference with function in the nerves resulting from anoxia

BURNING AND "PINS AND NEEDLES" are occasional complaints and are often present when the small distal vessels are obstructed. Trophic changes may be present, and the affected area is often hyperaesthetic and frequently ruberose.

Swelling of an extremity.—This is an unusual presenting sign but when it occurs is due to deep vein thrombophlebitis, but it is seen not infrequently in the later stages of the disease. It may then be due to excessive exudation from stagnating capillaries, persistent dependency, a position assumed to ease rest pain, or rarely to thrombophlebitis of the deep veins of the limb (Fig 268). When an unhealed ulcer or paronychia is present, infection and lymphangitis play their part in the production of oedema. Swelling occurring late in the disease is a serious sign implying a threat to the life of the limb

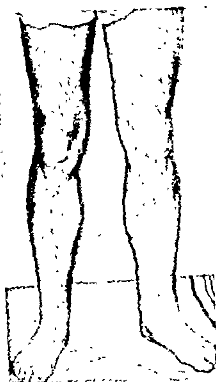


FIG. 268

Deep thrombophlebitis occurring as a presenting symptom in a man of thirty-seven years who within six months developed signs and symptoms of arterial ischaemia.

LEVEL FIRST AFFECTED

The diagnosis of the early distribution of the disease is based on the history and clinical features of the particular patient and is supported by arteriograms in some. Intermittent claudication with colour changes in the foot varying with dependency and elevation, without trophic change distally, together with an impalpable popliteal pulse indicate a femoro-popliteal thrombosis, but it is very probable that some of these patients also have disease of the tibial vessels. A similar clinical picture with a palpable popliteal pulse is taken to indicate primary tibial disease When patients present with a Raynaud phenomenon, painful ulcers, persistent rubor or incipient gangrene of digits with a pulse palpable at the wrist or ankle the disease is considered to be of a distal ...

... whereas it was distal in 36 8 per cent of patients. The hands were involved at some stage of the disease in 34 per cent. of cases, and in 13 per cent. symptoms were restricted to the upper limbs at the time when the patient first presented

Progress

The disease advances in episodes separated by period of inactivity of a few months to ten years or more. Sometimes the hope grows that the disease process has stopped, but there is no method of making sure that this is so When one lower limb is affected the contralateral limb is likely to be affected too, though often at a later date. Similarly when the upper limb is affected, it is usual for the disease to become bilateral in due course (Figs. 269 and 270).



Fig. 269
Thromboangiitis obliterans in a man aged forty-five. There is an ulcer on the great toe of the right foot, a finger has been amputated from the right hand; and there is an ulcer on the middle finger of the left hand

The time which passes after the first symptom and before the development of major gangrene varies greatly, and of course in some cases gangrene does not occur, but the average time for its onset is five years from the first appearance of symptoms. In rapidly progressive cases digits and even a major part of one or both lower limbs may be lost within a year of the first symptom. If there is a combination of proximal and distal disease in the same limb major gangrene is highly probable.

Although symptoms of proximal disease are frequent at first, as the disease progresses distal involvement occurs with an early onset of rest pain, persistent colour changes, ulcers on digits, and often gangrene. Primary distal disease ascends the limb until in some instances both femoral pulses may be impalpable. In two of our patients there is reason to suppose involvement of the internal iliac arteries or even the aorta, shown by absence of femoral pulses and inability to maintain an erection (p. 381) In the upper limb distal rather than proximal disease is more often first to occur. Generally it seems that the younger age group develop distal disease which tends to be more rapidly progressive than in the older group when proximal occlusion occurs more commonly, and when progression is slower.

About 20 per cent. of patients present with symptoms suggestive of sudden arterial occlusion, indistinguishable from that due to arterial embolism, with pallor, coldness and loss of distal pulses.[7] Sensory paralysis of a "sock" distribution occurs sometimes but is rare, as the obstructed segment of artery is generally short, and collateral arteries at this stage unaffected Symptoms of severe ischaemia generally improve rapidly with conservative treatment as

collateral vessels enlarge, leaving in their wake intermittent claudication, and perhaps positional colour changes. A massive gangrene is rare as a primary phenomenon, and only occurs where the popliteal artery and its branches are suddenly obstructed

We find it convenient to recognise five clinical types of the disease:—

1. *The progressive type* in which the disease advances in episodes. Episodes may occur at intervals of weeks or years, and gangrene may result after a few months, or several years, or many never occur.



FIG. 270
Bilateral affection of the hands in thromboangiitis obliterans

2. *The non-progressive type* in which the disease appears to become stationary with permanent mild ischaemic symptoms, although it is impossible to assert that there will never be any further incidents.
3. *The acute arterial occlusion type* in which there is sudden occlusion of a major vessel Diagnosis of thromboangiitis obliterans in this type of case is often impossible without prolonged observatio
4. *The*
   it so
   case
   ...ography there has been some degree of arterial obstruction in the digital arteries.
5. *Recurring superficial thrombophlebitis* in which there may be no arterial evidence of disease, often for years.

DIAGNOSIS

Recurring superficial thrombophlebitis suggests thromboangiitis or visceral cancer. If microscopical examination of an excised segment of affected

vein reveals an inflammatory reaction as opposed to a simple bland thrombosis, then *thromboangiitis obliterans* can be diagnosed confidently (Figs. 271 and 272). When other symptoms present it is necessary first to establish their origin in arterial occlusion, and then to differentiate the conditions which give rise to this. Ischaemia should be considered when there is recent coldness of a foot or hand, a Raynaud phenomenon, pain in the calf or foot on exercise, failure of a paronychia to heal or when a digital ulcer persists. Excessive fatigue in a lower limb after a walk, with rapid relief on resting, may be the earliest

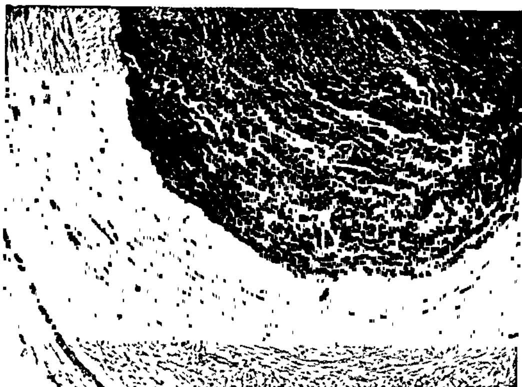


FIG. 271
Simple thrombosis in a superficial vein (*Angiology*.)*

symptom of muscle ischaemia before the cramping pain of intermittent claudication becomes evident. Intermittent claudication of the muscles of the foot is often first seen in foot clinics, the patients being treated for foot strain, arthritis or rheumatism Sometimes an arch support has been prescribed or physiotherapy recommended The pain however in these latter conditions does not show the same relation to exercise and persists after resting. Pain in the hand, particularly on writing, may signify claudication in the hand muscles *Many cases come to light after inexpert chiropody has produced ulcers which* fail to heal. Raynaud's phenomenon in an extremity occurring for the first time in a male in the second, third or fourth decades is usually due to thromboangiitis obliterans though it can also occur for the first time in patients of this age group after use of a *vibrating tool, following injury or frostbite* and

* LYNN, R. B. (1953). *Angiology* 4, 374

with one of the *collagen diseases.* The history will exclude the first three. but collagen disease especially *scleroderma* may be difficult to exclude. The presence of thickening or loss of resilience of the digital skin, dysphagia, sclerosis of lungs, heart or gastrointestinal tract, and alteration in the albumin-globulin ratio in the blood with a raised erythrocyte sedimentation rate indicate scleroderma but sometimes prolonged observation may be necessary before the diagnosis can be established with certainty; thromboangiitis itself has in fact been considered to be one of the collagen diseases.[38]



Fig 272
Superficial thrombophlebitis in a patient with Buerger's disease. There is an inflammatory reaction throughout the wall of the vein (*Angiology*)*

Polyarteritis nodosa may give rise to digital gangrene, but there is generally fever and other disturbances as optic atrophy, deafness, vertigo, abdominal disorders or evidence of generalised infection If the condition is suspected, muscle biopsy should be done, but this will only be of value if typical lesions in the vessels are found, and a negative result is without significance.

Functional disorders of the circulation which may mimic obliterative arterial disease include *acrocyanosis, livedo reticularis* and *erythromelalgia.* Persistent cyanosis in response to cold, atrophy of the digital skin and evidence of a stagnant peripheral circulation, is seen as a late result of acrocyanosis and livedo reticularis, conditions of obscure origin, associated with functional narrowing of the lumen or the arterioles (Chap XVI) They affect in some degree all the digits of the hands as well as those of the feet, and are

* See note on p 446.

often accompanied by rarefaction of the bones of the distal phalanges. There may be a patch of superficial gangrene of a toe in these conditions, but pain is absent, and pulses at the ankle and wrist are full. Diagnosis from thromboangiitis obliterans may be difficult but involvement to some extent of all four extremities, lack of pain, and relief of symptoms on reflex heating or peripheral nerve block should indicate the true diagnosis.

A bright rubor may occur as a symptom of *primary erythromelalgia* but in this condition there is a burning sensation of the part, the pulses are full and the discomfort is always relieved by cooling on immersing the feet in cold water. The disease is symmetrical in incidence. Hyperaesthesia occurs in erythromelalgia as it does sometimes in thromboangiitis obliterans of the distal type.

Once the symptoms have been shown to be due to organic obstruction, it is necessary to differentiate between *atherosclerosis* and thromboangiitis obliterans as the cause. If the patient is a male between twenty and forty years old; if colour changes in the digits tend to remain unchanged by posture and not to pale with elevation and darken with dependancy; if trophic changes are present; if there is evidence of disease in both legs *and also* the upper limbs; if there is a Raynaud phenomenon, *and if in addition* there has been a history of superficial *thrombophlebitis*, then the diagnosis of thromboangiitis obliterans is clear. *If on the other hand* the patient is over the age of fifty; if there is evidence of thickened, tortuous or calcified arteries; if rest pain is not a marked feature; and if colour changes are moderate or absent or only present on changes of posture, then a diagnosis of atherosclerosis can safely be made

FIG. 273
Buerger's disease Multiple minute collaterals are apparent

Hypertension, diabetes and a plasma lipoid content above 650 mg. per 100 ml. would suggest atherosclerosis

The chief difficulty of diagnosis between atherosclerosis and thromboangiitis obliterans is in patients between forty and fifty years of age and in



FIG 274
Buerger's disease The most distal vessels of the foot are extensively involved Collateral vessels are themselves affected The same limb as that shown in Figure 273

these a firm diagnosis may be exceedingly difficult; sometimes there may be evidence of calcification even in a limb the seat of thromboangiitis obliterans

Arteriography is of considerable value Involvement of the tibial vessels and the small vessels of the foot; the presence of large numbers of minute collaterals, the larger collaterals being affected by the disease, a smooth

outline of unaffected vessels; and absence of constriction or nipping at the origins of any patent larger collaterals suggest thromboangiitis (Figs. 273 and 274). Involvement of the femoro-popliteal vessels with rather patchy obliteration of tibial vessels; the presence of large dilated collaterals; roughening of the intima with constriction of the origins of the collateral vessels suggest atherosclerosis (Figs. 275 and 276). When the femoro-popliteal artery is the first and only vessel to be obstructed absence of roughening of the intima of vessels which are patent indicates thromboangiitis rather than atherosclerosis, but in these cases the diagnosis may remain doubtful until such time as other evidence of disease occurs (Fig. 277).



FIG 275
Atherosclerosis. There is irregularity of the femoro-popliteal trunk Collateral vessels are larger and less numerous

In many patients the diagnosis can only be established after microscopical examination of an excised segment of vessel, often the dorsalis pedis artery, or a segment of vein the seat of superficial thrombophlebitis.

When the initial symptom is that of acute arterial block, other causes of sudden arterial obstruction may have to be excluded.

In the case of *arterial embolism* some source for the clot usually reveals itself, a heart the seat of auricular fibrillation or at least mitral stenosis, or frank heart failure or an aneurysm of the aorta. *Arterial thrombosis* in atherosclerosis, when it is sometimes precipitated by a complicating condition such as an infective fever, or an injury, or the effects of a surgical operation, or some such blood disease as polycythaemia vera or a leukaemia The so-called *primary arterial thrombosis* or *spontaneous monarteritis* appear to be doubtfully specific conditions and in general it is wiser to reserve the diagnosis until the patient has been kept under observation for many years.

The vascular symptoms of *cervical rib or superior thoracic outlet syndrome* may present considerable difficulty and the demonstration of a cervical rib is by no means firm evidence that vascular symptoms on the side of the rib are due to the presence of the rib.

A postman of forty-two years of age complained of digital paraesthesia and Raynaud phenomenon of the first and second fingers of the left hand Though X-ray showed no evidence of cervical rib there was some tenderness in the supraclavicular region, and, though no sensory loss could be demonstrated in the left hand, there was no clinical evidence of organic obstruction of the vessels of the

forearm or hand. It was first considered that this patient's symptoms must be due to his habit of carrying his postbag slung from his left shoulder, with consequent strain at the thoracic outlet He was advised to change the weight of the bag to the other shoulder, and this eased his symptoms, yet two years later he reported with intermittent claudication, colour changes and coldness of the left foot. At this time the left ulnar pulse, previously palpable, could no longer be felt, and there were no palpable vessels at the ankle joint. A presumptive diagnosis of thromboangiitis was then made



Fig 276
Atherosclerosis The distal vessels are unaffected and the main vessels well filled. The dorsalis pedis artery is obstructed The same limb as that shown in Figure 275

In ...
tend
hand ... is uncommon Vascular symptoms in the hand should of course never be ascribed to thoracic outlet syndrome until a full examination of the peripheral circulation has been made. The various manoeuvres designed to obliterate or diminish the radial pulse, such as hyperextension of the neck and ... obliterans involvement of the



extension and rotation of the neck towards the site of the lesion are not dependable as evidence of thoracic outlet syndrome. Such procedures often produce diminution of the radial pulse in normal individuals. Recumbency in bed for some days will generally relieve symptoms in thoracic outlet cases but they may be temporarily effective also in thromboangiitis. The most important differentiating feature is the presence of other evidence of thromboangiitis obliterans.

In Britain *ergotism* is practically unknown but in those countries where it does occur it may be confused with thromboangiitis. Ergotism may result not only from the ingestion of infected rye bread, but also from the persistent therapeutic use of such drugs as ergotamine tartrate given for migraine or jaundice. The vascular effects of ergot are usually symmetrical in incidence and generally accompanied by keratitis, gastro-intestinal symptoms, and mental confusion.

Ulcers in the extremities, hypoaesthetic as a result of *syringomyelia, peripheral neuritis* and *tabes dorsalis* may give rise to difficulties, but pulses are present and ulcers are painless. Neurological or serological evidence of the responsible disorder can be obtained

TREATMENT

Once vascular thrombosis has occurred an irreversible state is established Although with time there may be some recanalisation, the reparative effect of this is insignificant Treatment therefore has to be directed towards these ends: —

FIG 277

There is nothing in the arteriogram to suggest atherosclerosis *This might be* termed primary popliteal thrombosis, or spontaneous monarteritis

1. The prevention of progression of the disease.
2. The care of the ischaemic limb.
3. The development of collateral pathways.
4. The management of gangrene

The prevention of progression of the disease.—The nature of the disease is such that, in the chronic type at least, there are periods of activity interspersed with periods of quiscence which may be of many years' duration. There is also said to be a distinct tendency for the disease process to die out, but it is difficult to distinguish permanent arrest from an inactivity that is only temporary This tendency of the disease to undergo quiscence or even arrest is responsible for the claims that have been made from time to time that some particular management is curative. Since the aetiology of the disease is unknown a rational treatment, with the intention of cure, is not available.

The effect of smoking in thromboangiitis obliterans in particular and in obliterative vascular disease in general, has been discussed previously, and although there is no final proof of its deleterious effect, there is sufficient clinical evidence to prohibit the use of tobacco in this condition. It is usual to advise the patient to stop smoking finally and completely (p 434).

Anticoagulant therapy with heparin and tromexan is indicated in acute thrombotic incidents affecting major vessels and tromexan should be continued for a month. Wright *et al.*[39] have shown that recent arterial thrombosis may be not only limited in extent but even resolved by prolonged tromexan therapy, yet it must be confessed that there is no available evidence of its value in thromboangiitis obliterans The continued use of anticoagulants as a prophylactic against thrombosis seems to be impracticable.

The injection of foreign proteins[40] particularly typhoid vaccine[5, 41] was at one time used with apparently good results in the treatment of rest pain or small painful ulcers but it has no effect in the acute progressive type of case, nor is it of value in relieving claudication in the milder case. The effect of the treatment is based on the fact that fever causes a maximal peripheral blood flow. It is suggested that an initial dose of 5,000,000 dead organisms is given and repeated at intervals of three days with a view to raising the mouth temperature by about 2 - 3°F, and the dose is adjusted to produce this effect Ulcers sometimes heal, and rest pain may be relieved under this treatment The increased blood flow which can be obtained by artificial pyrexia is less localised, less controlled, less permanent, and on the whole no less disturbing to the patient than that which can be obtained by sympathectomy

On the unproven supposition that there is haemoconcentration in thromboangiitis, the intravenous injection of hypertonic solution of 3 5 per cent sodium chloride, in quantities of 300 c c every few days for several months, has been recommended and practised[42] but the principle on which the

treatment is based has not been proved to be true and we have no experience of it.

There seems in fact to be no known method of preventing the progress of the disease with certainty, yet it does undoubtedly appear that those who abandon smoking have a better chance of remission or even of arrest of the disease, than do those who continue to smoke.[7, 41, 42]

It is generally wise to explain to the patient the nature of his disease in order to secure co-operation in treatment. Intercurrent disease must be treated, especially any anaemia, as when the blood flow through a part is defective the anoxia consequent on the deficient blood flow is exaggerated if the oxygen content of the blood is low.

The care of the ischaemic limb.—The patient must be instructed in the care of the feet. They must be kept clean with soap and water, particular care being taken of the interdigital clefts. Soaks in potassium permanganate 1: 10,000 on alternate days discourage dermatophytosis. The nails must be kept clean and be carefully cut. It is wiser not to cut corns or callosities, but rather to adjust the footwear to avoid pressure.

Socks must be smooth, and shoes free of irregularities and projecting nails. The feet, which are often uncomfortably cold are not permitted the comfort of a hot water bottle at nights; it is safer only to cover them with a sheet. In the early stages of the disease, if distal ischaemia is not severe and rest pain is absent, exercise is permitted within the limits imposed by the pain of intermittent claudication, and this will encourage the collateral circulation. Extremes of temperature are to be avoided. No form of physiotherapy such as diathermy, heat or massage has any place in treatment, and is harmful.

Any injury or abrasion, however slight, deserves special treatment, including rest in bed until the wound has healed. Strong antiseptics must be avoided, and a dressing of Bradosol (Ciba) 1: 2,000 is valuable as it is mildly antiseptic, does not adhere and is harmless to the tissues. Locally applied antibiotics, especially penicillin, may lead to extension of the lesion as a result of skin sensitivity.

Buerger's exercises, consisting of elevation of the affected limb to 90° for one minute, followed by dependency for one minute, followed by rest in the horizontal position for two minutes, the series being repeated for a period of twenty minutes at a time, and carried out several times a day, have been recommended with the object of emptying and filling the vessels alternately It is difficult to evaluate the effect of these exercises and they are not now commonly employed, but they may have some psychological value Other physical measures such as the oscillating bed and intermittent venous occlusion do not seem to have any positive value and may even be harmful.[43]

In more advanced ischaemia, and during periods of exacerbation of the disease rest in bed in a warm room or hospital ward is necessary. In order

to avoid swelling, affected limbs should not be much depressed below the horizontal. Nevertheless some degree of dependency is desirable and raising the head of the bed on 6" blocks is adequate to secure the effects of gravity, without causing any undue tendency to swelling.

The limb must on no account be artificially heated as not only is metabolism accelerated with consequent demand for a greatly increased blood supply which is not available, but also the ischaemic tissues are readily burned with possible gangrene in either case, a result which is frequently seen after contact with a hot water bottle or after the use of a radiant heat cradle. On the other hand local cold causes a vasoconstriction, and must be avoided. In acute cases a proper temperature is achieved with the patient lying in bed with the coverings supported by a bed cradle, and left open below, provided the temperature of the room is about 60°C., the usual ward temperature.

TREATMENT OF SEPSIS.—Ulcers occur spontaneously or after trauma and frequently burns. They are almost always painful. Antibiotics should not be applied locally, but may be given parenterally, although the paucity of the circulation in the region of the ulcer minimises their effects. Moist dressings and soaks remove crusts and assist free drainage. Inflammatory products retained by sloughs or beneath a nail must be evacuated, by removing dead tissue or the overlying nail. A slough, often hard and leathery, can be snipped away with scissors where it is not attached to the deeper tissues, and a nail can usually be trimmed sufficiently to relieve tension. Sometimes perforation of a nail by an eye trephine in several places may facilitate its painless removal piecemeal with scissors, but this can only be done where the nail is separated from its bed by pus (p. 400). The relief of pain after the evacuation of pus is often dramatic, and the ability of the tissues to form pus indicates a blood supply sufficient to complete the healing process.

The only operations, apart from amputations, allowed in ischaemic digits are those which can be done *painlessly*, which mean that tissue which is already dead is the only tissue which must be removed. Anaesthetics are dangerous, general as they might allow interference with living tissues, and local as they would certainly precipitate gangrene.

Development of the collateral circulation.—During periods of exacerbation of the disease the patient is nursed in bed, with the affected part cool and slightly dependent; the rest of the body is kept warm, even to the point of slight discomfort. This will induce a measure of peripheral vasodilatation. Deep sleep also has an important vasodilating effect and should be encouraged by the careful use of suitable barbiturates.

The most valuable vasodilator drug in thromboangiitis obliterans is Priscol in doses of 50 mg. three times daily, and it is probably of most value in patients suffering from a recent incident, particularly a sudden proximal occlusion; it is of no value when pain is severe and when ulcers or gangrene are present. Alcohol is useful, not only for its vasodilating but also for its

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and should be advised. Furthermore the dry foot after the operation inhibits dermatophytosis.

When the disease first presents as an acute arterial occlusion of a major vessel conservative treatment is indicated whilst the signs of ischaemia are gross. During this phase such measures induce a degree of peripheral vasodilatation similar to that achieved by a sympathectomy, and the risk of superadded thrombosis resulting from circulatory disturbances attendant on an



FIG. 278
Post-mortem *arteriogram* of a foot amputated for thromboangiitis obliterans. Little could be expected from sympathectomy in such circumstances as the most distal vessels are obliterated

operation are avoided. The circulation nearly always recovers without gangrene, except in those rare cases where a massive thrombosis of the femoro-popliteal artery and its branches has occurred. The question of a sympathectomy is considered after a few weeks when the interference with the circulation has been assessed.

Sympathectomy should therefore be done for symptoms of thrombo-angiitis, and not for the disease. [illegible]

[illegible] severe symptoms, particularly if [illegible] palpable popliteal pulse, sympathectomy is to be advised. In late cases, particularly when distal disease has been complicated by proximal disease—of the femoro-popliteal artery—or *vice versa*, and if the foot is the site of severe pain and persistent colour change, the prognosis as regards life

sedative effect and should be given in amounts suitable for the individual patient. Analgesic drugs must be prescribed with the greatest caution for addiction is easily induced in those who suffer from thromboangiitis. Pethidine is preferable to morphia though both are habit forming, but when analgesic drugs are required regularly, it is time to consider amputation.

SYMPATHECTOMY.—Sympathectomy has no effect on the pathological process of the disease in the vessels. Its effects are achieved only by a reduction of tone in those vessels which remain patent, thus increasing the distal blood flow.

In rapidly progressive disease it will have little chance of improving symptoms, as by the time improvement has occurred further incidents may have befallen the patient, and it becomes a race between the effects of sympathectomy and the advance of the disease. Nevertheless, whilst admitting doubt as to its efficacy in such cases, the operation should be done, as it is impossible to say when the disease may become inactive, often for long periods.

In recurrent superficial thrombophlebitis without any evidence of arterial obstruction, sympathectomy is unnecessary and should not be done

If the disease involves the femoro-popliteal artery only, symptoms of claudication predominate, and claudication is not often relieved significantly after sympathectomy. If, however, there are in addition feelings of coldness or numbness or particularly any trophic changes in the feet, or if the claudication distance is less than 200 yards, the operation is valuable.

The tibial vessels are most often the first to be affected, and claudication in the calf or foot with coldness and numbness distally is common. It is in this type of case that sympathectomy is of real value, and its benefits greatest, paraesthesiae being relieved, ulcers if present frequently healed, and claudication in the foot lessened or even cured.

When the smallest vessels of the extremities are diseased, the decision as to whether sympathectomy should be done depends on the degree of vessel involvement. In the most distal type, not only are the main digital vessels, but also the veins and often the collateral vessels obstructed by disease, and the circulation is almost stagnant, and little can be expected from sympathectomy, as the vessels that remain patent are often minute and tortuous (Fig. 278). This type of case can be recognised by the presence of marked skin atrophy, severe rest pain, colour changes which persist irrespective of posture and often an unhealed ulcer or patch of gangrene. Some degree of rest pain is relieved by sympathectomy, and patients who would be relieved by the operation enjoy relief by medical means, bodily heating, alcohol, barbiturates and vasodilator drugs, whereas if pain is only relieved by pain-relieving drugs, little will be achieved by sympathectomy.

In less severe degrees of distal involvement, with Raynaud's phenomenon, paraesthesiae and sometimes paronychiae or ulcers, sympathectomy is of value

Transmetatarsal amputations have no more place in thromboangiitis than in other conditions of arterial insufficiency. The wound of a transmetatarsal amputation may heal satisfactorily, but will be of poor nutrition, and functionally unsatisfactory. If amputation of toes alone does not leave a satisfactory stump, then a below-knee amputation is indicated.

MAJOR AMPUTATIONS.—Below-knee amputations can always be done if the popliteal artery is patent. If the femoral artery is obstructed the success of this operation is less assured A palpable pulsating collateral vessel over the medical condyle of the femur is a hopeful sign but is uncommon in thromboangiitis obliterans. If postural colour changes are present over the lower leg as well as the foot above-knee amputation will be demanded. If arteriography shows that there are adequate collateral vessels, amputation may be considered through the leg. If, however, there is claudication of the calf muscles at one hundred yards or less, it may be assumed that ischaemia is severe and that a below-knee operation is likely to fail in its purpose.

Amputations through the knee of the Stokes-Gritti type, though useful in atherosclerosis, are not advisable in thromboangiitis as the collateral vessels are likely to be diseased with resulting failure of the flaps to heal. The patients with this disease are, generally in the younger age group, and the prosthesis after amputation through the knee is not very satisfactory, for the artificial knee joint cannot be placed in its proper position, and there is no control over the joint The prosthesis is in fact no more satisfactory than is a rigid peg-leg

ABOVE-KNEE AMPUTATIONS.—This procedure is necessary where no lower amputation would be successful In thromboangiitis the stump after this amputation has always healed in our experience and remains healed, but in one patient in whom the disease has spread to involve the aortic bifurcation, the stump is cyanosed and ischaemic.

PROGNOSIS

The ultimate outlook in any particular case of thromboangiitis obliterans is always difficult to estimate on account of the variability of remissions between active and quiet phases of the disease. Certain facts appear, particularly that either distal disease *or proximal* disease alone will not usually jeopardise the life of the limb, but distal *and* proximal disease almost invariably demand a major amputation. Of bad prognostic significance are persistent colour changes and *pain in the toes or foot* It is very unusual to lose a hand, although digits may demand [illegible] of our forty-one patients only [illegible] to ar[illegible] ave never had occasion of o[illegible] limb is concerned ten [illegible] undergone major amputation, and in four of these amputation has been bilateral. Six of fourteen amputations have been above-knee, and eight below-knee Four major amputations have been done within

of the limb is poor, and if after a week or two of medical treatment there is no improvement of the local condition, then amputation should have preference over sympathectomy.

Sympathectomy as an adjuvant to amputation is a valuable measure. Amputation of a digit or digits, and a below-knee amputation in doubtful cases, may be undertaken with more hope of success if sympathectomy is done at the same time, as the increased blood flow is most marked in the few days following the procedure—when the healing process is most active.

OTHER SURGICAL MEASURES.—*Ligature of the femoral vein, excision of* thrombosed segments of artery[44, 45] and unilateral adrenalectomy[46, 47] have been advised, but few consider *these measures to be effective.* Venous ligations may interfere with the remaining circulation by back pressure and oedema; the surgical approach for arteriectomy is liable to divide existing collaterals and the operation has not had significant success; and there seems no rationale for unilateral adrenalectomy. In our hands the replacement of thrombosed arteries by grafts has not been successful. We have performed the operation in two cases of femoro-popliteal thrombosis in this disease and no improvement followed in either case, the graft becoming obstructed within a few days in each patient, but a successful result has been reported by Hallén.[49]

The management of gangrene.—MINOR AMPUTATIONS.—Amputation of *a digit or part of a digit is indicated when an ulcer fails to heal; when pain* is severe and restricted to the affected digit and does not, or does not *significantly, spread on to foot or hand; in the presence of infected inter-*digital joints or osteomyelitis of the phalanges; or when gangrene is present. *A line of demarcation should be allowed to form, and if there is no excessive* atrophy of the skin of the palm or foot and colour changes if present vary *with elevation and dependancy, then healing is probable.*

Amputation of the middle three toes is more likely to be successful than is amputation of the great or little toe. Amputation of fingers is sometimes necessary but amputation of a hand has never been demanded in our experience. An infected metatarso-phalangeal joint may still be treated by a minor amputation, the head and distal shaft of the metatarsal being removed at the same time (p. 403). Arteriography of the hand or foot is helpful in guiding the surgeon, for filling of the palmar or plantar arch indicates that a minor amputation will probably be successful. Five of our cases have undergone nineteen amputations of some or all of the toes, excepting the great toe, with satisfactory healing in all but two. The great toe has been removed five times with healing in three cases and further major *amputation* at an early date in two. It is worthwhile taking some risk with regard to healing of the stump when digits are amputated, and a *sympathectomy* at the time of amputation is an important measure, unless it has been done previously. *Amputation of fingers has been successful in the* two patients on whom we have performed this operation.

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one year of the onset of symptoms, and these have all been in men under thirty years of age. In the others, the average interval between the onset of the disease and major amputation has been six and a half years, and the longest interval has been fourteen years. In patients followed for four years our amputation rate in the lower limbs has been rather more than 18 per cent.; this compares with an amputation rate of 32 per cent. of limbs,[8] and in 26 per cent. of patients,[9] in a fourteen year follow-up.

A major amputation rate of 7·5 per cent. has been reported by Silbert[49] and a similar figure has been recorded from the Mayo Clinic, but these figures do not include amputations done before and after the patients' stay in a particular clinic. It has been found that 59 per cent. of patients followed throughout the course of their disease have some form of amputation within ten years of the onset of the disease, and half of these are major amputations.[50]

The major amputation rate has certainly diminished during the last ten years, perhaps from a better understanding of the natural history of the disease; from the more general adoption of local amputation of a digit together with lumbar sympathectomy; from insistence on abandonment of smoking, and from the proper care of ischaemic limbs.

Prognosis as regards life is again difficult to estimate and mortality rates of 14 per cent.[9] and 10 per cent.[8] over periods of fourteen years have been attributed to the disease. Myocardial infarction, mesenteric thrombosis, cerebral haemorrhage and extensive gangrene are reported causes of death in thromboangiitis obliterans though there is little evidence that the visceral vessels have been involved by this disease, but it does appear that such vascular accidents are more common in association with thromboangiitis obliterans than in patients not suffering from this complaint.

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dilate immediately, and the most valuable of these are the ones that return the arterial flow most directly to the main trunk (Learmonth[13])—muscular collaterals are not very valuable in this respect. Less direct collateral routes, developed by the dilatation of small vessels, come into action more slowly. Once the embolus is firmly impacted, thrombosis may occur either proximal to it or distal to it or at both extremities, and for this process Richards[1] applies the term "consecutive thrombosis," reserving the term "secondary thrombosis" for the thrombosis which occurs after embolectomy. Atherosclerosis in the affected vessel and its branches may prevent the dilatation of collateral channels and progressive thrombosis or even spasm in the main vessel may occlude the mouths of branches important in alternative collateral routes. The importance of spasm in exaggerating the effects of embolism is disputed. Pickering[15] gives as his opinion that "the idea of severe and localised contraction of an artery, vascular spasm, occurring in the absence of a recognisable stimulus, is entertained too freely and uncritically in current thought and writing." Richards[16] has examined this problem in detail and considers that there are three phenomena which seem to indicate that arterial spasm does occur *in association with embolism: (1) the finding of constricted* arteries at operation;[17, 18, 19] (2) the delay in the return of pulses after successful embolectomy;[20] (3) the occurrence of "pseudo-embolism," in which all the features of embolism except the embolus are present.[13, 21, 22] This condition of pseudo-embolism is thought to be due to an embolus temporarily occluding a main artery, and then slipping into a branch of less importance than the main artery, but continuing, by the spasm which it evokes in the arterial tree, to produce the same effects as if the main artery were still occluded.

CLINICAL FEATURES.—*Pain is usually the first* symptom. *Usually sudden*, it may be gradual in its onset and there is no distinction between the pain of thrombosis and the pain of embolism. The pain is diffuse, cramp-like, continuous and referred to a level usually some distance below the point of occlusion. The initial occlusion is probably sometimes painless, with a latent interval between the moment of impaction and the onset of the pain. Even a pain of sudden onset may be a delayed pain, and the moment of embolism cannot always be precisely deduced, though in most cases the pain is probably immediate; arteriography performed in the leg under local anaesthesia is usually productive of immediate pain.

The cause of the pain of embolism is now disputed. It was long thought that pain was due to impaction of the embolus in the artery and consequent stimulation of the arterial walls, but Lewis[23] advanced strong arguments for the belief that the pain of embolism was the result of ischaemia of muscle. His chief arguments were: (1) pain is not invariably the initial symptom of peripheral embolism; (2) the occlusion of non-muscular organs such as the brain is painless; (3) pain is felt not at the site of impaction of the embolus, but distally, and usually in a muscular portion of the limb; (4) when embolectomy is successful, pain is relieved not by removal of the embolus,

CHAPTER XII

EMBOLISM OF PERIPHERAL VESSELS

PERIPHERAL embolism[1] is the occlusion of a peripheral artery by a clot usually from a distant source. An embolus may pass to the systemic circulation from the left auricle in auricular fibrillation, from the left auricle or ventricle in coronary infarction or congestive heart-failure, from the mitral valve in endocarditis, from an atheromatous plaque on the aorta or from a mural vegetation in aneurysm. Embolism used not to occur from the fibrillation of toxic goitre unless mitral stenosis was present also, but it does sometimes occur now under thiouracil. In atherosclerosis a portion of clot may become dislodged and impacted lower in the affected arterial trunk. Groth[2] has described "tumour embolism" of the left femoral artery in a patient suffering from lung metastases after amputation of a sarcomatous limb. The embolus, of malignant giant-cell tissue, was removed with re-establishment of the circulation Most tumour emboli are microscopical but massive tumour embolism has been described in the brain,[3] in the kidney,[4] in the spleen,[5] in the lungs,[6] and in the liver.[7] An unique case of embolism in which a large clot at the aortic bifurcation invaded by embolic cells from a lung carcinoma, produced gangrene of one lower extremity, is recorded by Till and Fairburn.[8] "Paradoxical embolism" may occur if the foramen ovale is widely patent, a clot passing directly from a systemic vein to the systemic arteries. The obliquity of the foramen ovale makes it a little difficult to understand the mechanism of paradoxical embolism, but a case has been described in which the primary clot lay in the actual foramen,[9] and Ingham[10] saw seven cases of thrombus in transit through the foramen. Cases of paradoxical embolism in which the travelling clot has originated in the pulmonary veins have been recorded [1, 11] Exceptionally a bullet lodged in the left heart may pass into the aorta and act as an embolus in one of its larger branches [12]

The common sites of lodgement are the aortic, femoral, popliteal and brachial bifurcations An embolus temporarily lodged at one arterial bifurcation may become detached and lodge at the next lowest bifurcation, or an embolus saddled across a bifurcation may break into two halves, one of which may be carried into each trunk. The effects of embolism depend upon (1) the degree of obstruction produced at the site of lodgement; (2) the level of embolic obstruction; (3) the development of collateral circulation; (4) occlusion of the mouth of collaterals by the embolus; (5) the addition of secondary thrombus; (6) the condition of the arterial walls; (7) the degree of secondary spasm in the arterial tree distal to the level of lodgement of the embolus; (8) the reaction of the heart, and (9) the presence of infection. Some collaterals

pain in the foot and lower leg usually, movements may be lost completely in the toes but seldom completely at the ankle; numbness, coldness and discoloration are usually limited to the foot, gangrene if it occurs seldom amounts to the loss of more than a toe, and embolism at this level may be symptomless. Axillary embolism gives pain sometimes in the whole upper extremity; fingers and wrist are often paralysed and the elbow weak; the distal forearm and hand may be anaesthetic, but gangrene seldom affects a wider area than the fingers, and rarely the whole hand. Brachial embolism, if it gives symptoms at all, gives pain in hand or forearm, weakness of fingers but no complete paralysis, numbness and discoloration in the fingers, hand and lower forearm, and gangrene of the terminal phalanges; at this level, as at the popliteal bifurcation, embolism may be symptomless.

TREATMENT.—Learmonth[13] advises that however early a case be seen, anticoagulant therapy be tried for two hours—dramatic improvement may occur within that period If after two hours it is obvious that complete occlusion has occurred, embolectomy is performed, but the operation is usually hopeless if done more than ten hours after the onset of the pain, for thereafter adherence of the clot to the vessel wall becomes increasingly dense and all hope of a successful embolectomy must certainly be abandoned if a period of thirty hours has elapsed Muscle may be considered usually to be dead, and the nerve tissue of the limb too, after ten hours or less of complete ischaemia, and probably conservative measures are to be preferred after this interval. Twelve hours of complete ischaemia is followed by gangrene in more than 50 per cent of cases, and all cases of ischaemia of this duration have severe impairment of function even if the limb survives. In the upper limb, operation is virtually never required; spontaneous recovery is common even without any treatment at all, for pre-formed collaterals are more numerous in the upper limb than in the lower.[25]

Heparinization is the sheet-anchor of conservative treatment, and is begun immediately in later cases, immediately after operation in cases where operation is done, or, as Learmonth advises, in all cases for a trial period of two hours. Patients likely to go to operation are best maintained on heparin alone so that protamine may be successfully used if required. For details of anticoagulant therapy see Chapter XIX

Concomitantly with heparinization all measures for the treatment of incipient gangrene (see p. 390) are instituted.

At embolectomy, the affected vessel is exposed under local anaesthesia at the point of lodgement of the embolus. After [illegible] established [illegible] passed rou[illegible] covered cl[illegible] is remove[illegible] [illegible] out with the fingers. After it is extra[illegible], first the upper and then the lower clamp is loosened so that the blood stream may wash out any residual fragments of clot; distal extension

but only when the circulation is restored. Richards[16] *distinguishes*, as Rykert and Graham[24] did, between two distinct types of pain in embolism: an initial pain which is sharp, worse at the onset, and felt at the site of occlusion, and a later pain which comes on gradually, but rapidly becomes more severe, situated distal to the site of occlusion and aggravated by movement of the limb. Richards agrees with Lewis that ischaemia is the principal cause of pain in embolism, but doubts whether muscle is always the tissue from which the pain arises; pain is sometimes most severe on the dorsum of the foot or in the palm of the hand, which are relatively non-muscular areas. He considers that while the initial pain of embolism, when it occurs, may be due to sudden arterial distention, the later pain is certainly due to ischaemia. The pain is associated with and sometimes preceded by, a feeling of numbness and coldness which may proceed to stocking anaesthesia. Sometimes, even in the aorta, embolism is entirely painless, and may even occur during sleep.

At the site of occlusion the artery may be felt distended with firm clot and pulseless. Tenderness may or may not be elicited immediately, but it is always present after a few days. Distal pulsation is lost and returns only exceptionally, and oftener in the arm than in the foot. Care should be taken, however, not to place too much reliance on the detection of pulsation in the neighbourhood of an embolus, for sometimes pulsation may be transmitted from the level of the clot to the empty vessel below it. The distal part of the affected extremity, initially pale, gradually darkens in hue, becoming first mottled and then uniformly cyanosed. The colour changes begin some inches below the obstruction and increase in intensity proximo-distally. The distal parts may proceed to gangrene. There is a centripetal weakness and flaccidity of muscles, anaesthesia, numbness and progressive fall in temperature. The actual level of the occluding clot can be estimated by the level of loss of palpable pulsation, and by oscillometry.

The symptoms vary with the vessel involved In general, the larger the vessel blocked the greater the resultant disturbance. In aortic embolism pain is distributed to both lower limbs and sometimes to loin or lower abdomen; there is loss of movement from the knee or even the hip downwards; numbness, coldness and discoloration extend from mid-thigh or hip to toes; gangrene, often massive, is of feet, or legs, or still more extensive, and I have seen it extend to the waist before death; the symptoms are roughly, seldom exactly, symmetrical, for the clot as it straddles the bifurcation does not straddle it symmetrically. Haematuria may occur if the hypogastric vessels are affected, and, as the secondary clot spreads, it may lead to intestinal infarction and finally to anuria. The symptoms of aortic embolism may be precisely reproduced by dissecting aneurysm of the aortic arch, which, extending to branches of the aorta, may even simulate axillary, femoral or carotid embolism. In femoral embolism pain is restricted to foot and leg; movement is lost in foot and toes; numbness, coldness and discoloration do not extend above the knee, and gangrene affects the leg and foot. Popliteal embolism gives

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of thrombus is the main threat to the limb; proximal extension, to the aortic bifurcation and beyond in the case of the lower extremity, is the main threat to life. After removal of the clot, the lumen of the vessel is washed with heparin, the arterial wound is closed by interrupted sutures of waxed silk carried on a round-bodied silver arterial needle whose diameter equals that of the silk, and the arterial clamps and tapes are removed (p. 806).

Many successes are recorded after the operation of embolectomy, but it is sometimes difficult to tell whether recovery is due to operation or would have occurred without it. No cure is acceptable unless the distal pulses return within a few hours of operation and remain palpable. The operation rarely if ever does any harm to the patient, and probably never increases the risk of gangrene. Einar Key[1] performed 48 operations on 43 patients; several died of other causes but a good result was obtained in 39·5 per cent., and only 20·8 per cent. proceeded to gangrene. Warren and Linton[26] had an over-all case mortality of 38·7 per cent. in embolism at all sites, including those other than the limbs. Nearly 90 per cent. of limbs subjected to early embolectomy were saved, but such a series is difficult to assess against proper controls.

Since embolism may occur against a background of heart-failure, the basic cardiac condition may require treatment too. Auricular fibrillation requires particularly careful handling—quinidine may dislodge further pieces of clot from the auricle. Mitral disease with auricular fibrillation and peripheral embolism is very suitable for surgical intervention, and in these cases valvulotomy should be combined with excision of the auricular appendage.[27]

For aortic embolectomy[28] a midline sub-umbilical incision is suitable and a trans-peritoneal approach[13] is more direct than the extra-peritoneal approach of Murray,[29] though Murray found no difficulty with the extra-peritoneal route in five personal cases The proximal aorta and the distal iliac arteries may be controlled by special clamps[30] or by tapes. It is wise to incise the aorta itself just above the bifurcation rather than to open the iliac arteries "milking" the clot down from above and over from one iliac artery into the other. The aortic approach, aided by gentle "milking" just behind the clot, is the simplest method of removal. Long survival after aortic embolectomy is not to be expected for further embolic episodes are almost inevitable and cerebral embolism is often the ultimate cause of death, but many of the patients undergoing this operation, though in cardiac failure, have survived for more than a year.

I. A.

affected patients has suggested that it may be a degenerative process of vascular tissues with ageing Hutchinson[17] implied this when he stated that the condition was found in unsound, but not calcareous, arteries but the generalised nature of the arteritis renders his local theory of its cause untenable.

Bacteriologically, culture of the involved arteries at biopsy has revealed no specific organism consistently and those isolated have been considered by most to be contaminants *e.g* actinomycoses[5] Blood cultures have been universally sterile and all routine agglutination and serological tests have been negative.

CLINICAL FEATURES.—Non-specific granulomatous arteritis is a disease of old age, the average age being sixty-five years and, although a pathologically acceptable case has been reported in a twenty-two year old woman,[27] cases of patients under the age of fifty years are rare. Females predominate in the ratio of two or three to one and as far as can be ascertained the condition has not been reported in the coloured races.[21]

The clinical features can be divided into general and local. The constitutional symptoms are those of the subacute onset of a febrile illness in a previously well elderly person There is loss of energy and, invariably, weight loss with anorexia and a general malaise which may pass into a phase of depression and apathy leading to the mistaken diagnosis of a melancholic psychosis.[6] More than 70 *per cent* have an inconstant low grade fever, generalised myalgia and arthralgia being very commonly associated. Such constitutional manifestations may precede the appearance of localised symptoms of the disease by as much as a year and have been confused with diabetes, tuberculosis, psychosis and, when the weight loss has been severe, malignant cachexia.[31] In rare instances cerebral symptoms have predominated with vertigo, mental confusion, delerium and even coma leading to a diagnosis of brain tumour or cerebrovascular accident.[6]

The local symptoms depend upon the artery or arteries affected. The temporal artery is almost always affected at some stage in the disease and its superficial course leads to severe local effects Headache is a constant feature, frontal and temporal in distribution, unless the occipital artery is involved, when pain in the neck and back of the head is prominent. The headache is severe, throbbing, constant and is exaggerated by sudden movements or touch so much that contact of the head with the pillow is unbearable. Consequent loss of sleep may seriously affect health. At least half of the sufferers complain of pain on mastication which may be so trying as to cause limitation of diet[33]

Local examination is often disappointing and it may be hard to ascribe the debilitated state of the patient to the local findings The involved vessel,

CHAPTER XIII

ARTERITIS

THE term arteritis refers, by usage, to a variety of diseases which are associated with sterile, subacute inflammatory lesions of the peripheral and visceral arteries. Although the conditions to be discussed herein possess many clinical and pathological similarities the aetiology of most of them has not been established definitely so that it seems best to consider them as clinical entities until more definite data are at hand.[3]

It is not surprising that pathological similarities are evident in arteritis since arteries can respond to noxious agents of varied character with but limited types of reaction. Thus the same pathological type of acute arteritis can be induced by infection, exposure to cold, vasospastic drugs and hypersensitivity or allergy.[38] It follows, therefore, that the clinical picture associated can be equally variable and the demonstration of arteritis does not necessarily imply that the causative agent is bacterial since, as in other tissues, infection is but one of the causes of inflammation.

There has been a tendency to include the arteritides under the general heading of "collagen diseases." This has added nothing to our knowledge of the pathogenesis and, while indicating a common pathological attribute of the group, does not imply that its members are necessarily related to one another aetiologically. However, all these conditions are characterised by a widespread vascular and connective tissue abnormality which is characterised in each by certain dominating focal manifestations which serve as a clinical basis for the differentiation of one from the other.

NON-SPECIFIC GRANULOMATOUS ARTERITIS

This is an uncommon, febrile, self-limiting disease of variable duration and unknown aetiology A variety of names have been attached to the condition: temporal arteritis,[5, 6, 15, 16, 18] cranial arteritis,[21, 33] giant cell arteritis[4, 9, 13] and granulomatous arteritis of undetermined cause[7, 26] The first two of these do not reflect the generalised nature of the disease and the term giant cell arteritis is too vague for giant cells appear in other arteritides. It is suggested that the term non-specific granulomatous arteritis, qualified by the appropriate adjective, *i.e* generalised, temporal, cranial etc., is the best clinico-pathological description until more is known of the nature of the disease

AETIOLOGY.—The cause is not known. The possible aetiological agents include infection, allergy, the degenerative process of ageing and a generalised collagen disturbance. The clinical course and pathological picture are most

TREATMENT.—There is no specific treatment but recently remarkable relief of symptoms has been obtained from cortisone and A.C.T.H.;[1, 33, 39] the local and general manifestations rapidly subside but promptly relapse if the treatment is not continued for at least one month. The sedimentation rate is seldom

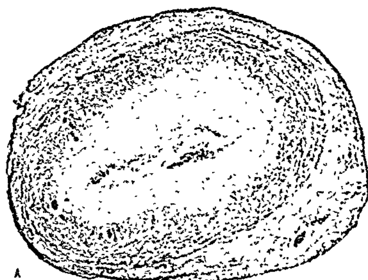




FIG. 279

A—Temporal artery showing trace of thrombus - thickened intima, cellular infiltration of media and fibrosis of adventitia. ×40 B—Junction of intima and media showing fragmentation of elastica, giant cells and cellular infiltration ×190.

(C V Harrison—Recent Advances in Pathology)

[illegible] hormones probably act by blocki [illegible] patient is [illegible]
as yet not understood Such an explana [illegible]
as for other " collagen diseases " whose r[illegible]ponse to these agents is similar.

if accessible as the temporal artery is, is thickened, tortuous, nodular and usually pulseless. The overlying skin is red, oedematous and tender and pronounced hyper-aesthesia is usual. The arterial involvement is usually patchy, only localised segments of the vessel being diseased.

Visual disturbances occur in almost half of the cases of temporal artery involvement and about half of these are left with total or partial loss of vision in one or both eyes.[4, 13] Mistiness of vision, photophobia, diplopia and finally blindness, which may be total or affect any field of vision, are the commoner complaints. Ophthalmoscopic findings are disproportionate to the visual loss but areas of retinal ischaemia and pallor are noted with rare haemorrhages and mild oedema of the disc ending in optic atrophy. These changes are the result of involvement of the retinal and ophthalmic arteries by the arteritis.

Laboratory examinations constantly show a hypochromic anaemia and an elevated sedimentation rate. The anaemia responds only to blood transfusion. A slight leucocytosis is common and there is no eosinophilia There is no demonstrable bacteriological or serological abnormality.

PATHOLOGY.—The histological picture is that of a low grade arteritis, affecting all the coats, in which the features are intimal hypertrophy, medial necrosis, associated with the formation of granulomatous tissue and the presence of multinucleated giant cells, and adventitial cellular infiltration (Fig. 279).[13] The intima is greatly thickened so that the lumen becomes a mere slit and although thrombosis may complete the obliteration it is not a usual feature. The media is the site of maximum change which includes cellular infiltration, necrosis and aggregations of giant cells of both the foreign body and Langhans type, associated with destruction and fragmentation of the internal elastic lamina. The inflammatory cells are chiefly lymphocytes and macrophages with a lesser number of plasma cells; eosinophils are rare. The perivascular connective tissue shows similar cellular infiltration and the vasa vasorum shows "cuffing" Aneurysmal dilatations are not seen. The multiplicity of arteries in which these changes have been recorded leaves little doubt of the generalised nature of the disease Temporal, occipital, ophthalmic, retinal, coronary, radial, ulnar, femoral, carotid, renal, mesenteric, iliac, subclavian, innominate, coeliac, pulmonary arteries and the aorta have all suffered.

PROGNOSIS.—Non-specific granulomatous arteritis is a self-limiting disease which usually runs a benign course of one to twenty-four months although of the 157 cases so far reported approximately 20 per cent. have been fatal. It is only fair to add that not all of these deaths have been attributable to the disease itself. The commonest cause of death is a cerebrovascular accident[4, 13] The generalised nature of the disease makes accurate prognosis uncertain but most cases recover and, although pulsations may return in the temporal arteries, visual impairment, due to involvement of the ophthalmic or retinal arteries, is permanent[13, 21]

antly in one organ or system polyarteritis may simulate some other disease of that organ or system. The picture may be so confusing that the diagnosis is not made during life.

Although no standard clinical description is possible there are some features that are very frequent. The onset may be gradual over a period of eight to twelve months or occasionally an acute fulminating course is run with death after a few days. Varying degrees of fever with a tachycardia out of proportion to the pyrexia are commonly noted. Loss of weight, anorexia, abdominal pain and hepatomegaly are frequent and may lead to a diagnosis of carcinoma of the stomach or colon. Hypertension is usual at some stage and is always present when the kidneys are extensively affected. The kidneys are the organs most frequently involved, with consequent albuminuria, cylindruria, haematuria and hypertension. In the more chronic forms of polyarteritis nodosa peripheral neuritis,[34, 29] chiefly of the legs, and visceral complaints tend to predominate. Subcutaneous nodules are present in many cases and a variety of skin eruptions may appear. Raynaud's phenomenon is not uncommon[10] and gangrene of the extremities has been reported.[12]

Polyarteritis nodosa may present as one of the following: a non-specific subacute or chronic pyrexial wasting illness; an atypical abdominal illness of long duration in which the diagnosis may be established by pathological examination of an excised gall bladder or appendix; primary renal disease, or a combination of polyneuritis and polymyositis most severe in the lower limbs.[29]

Laboratory examinations reveal a fairly constant polymorphonuclear leucocytosis but eosinophilia, often said to be a characteristic feature of the disease, is an inconstant finding. Hypochromic anaemia and an elevated sedimentation rate are frequently observed. Albuminuria is usually present and, less commonly, haematuria and cylinduria. The Wasserman reaction is characteristically negative.

PATHOLOGY.—Although any or all organs of the body may be affected the vessels of the kidney, heart, liver, gastro-intestinal tract (including the mesentery and pancreas) and the muscles are involved in order of descending frequency. The site of predilection appears to be the point of bifurcation of the smaller visceral arteries and arterioles.[40] The distribution is segmental and long stretches of the vessel on either side of the diseased segment may be normal. On rare occasions the accompanying veins are involved by a similar process.

[illegible] ed by a necrotising panarteritis [illegible]

[illegible] nodosa is that all [illegible] at the same time. In other words the lesions occur in crops. Classically the first stage is one of acute necrosis or degeneration. The inner part of the media or the subintimal region of the vessel is chiefly affected

Therapeutic resection of the affected segment of the superficial temporal artery permits an accurate histological diagnosis to be made and at the same time abolishes the local manifestations of the disease.[6, 7, 15, 16, 26] Perivascular infiltration with a local anaesthetic has a similar, but short-lived effect Unfortunately neither procedure may dramatically improve the constitutional symptoms. Antiobiotics have little or no effect on the course of the disease but one cure has been recorded after the administration of antihistaminic drugs.[26]

POLYARTERITIS NODOSA

This is a widespread, destructive, inflammatory-necrotising reaction of the vascular tree in which the smaller arteries and arterioles of any or all body structures are involved with consequent protean clinical manifestations. The condition is known by a variety of names—periarteritis nodosa, essential polyangiitis and polyarteritis nodosa being the more common ones. Polyarteritis nodosa is perhaps the least objectionable although none is exactly descriptive since, strictly speaking, it is a panarteritis and nodularity is by no means universal. Originally polyarteritis nodosa was considered to be a rare disease but the more frequent recognition of milder cases has shown it to be less rare than previously believed.

Aetiology —The aetiology has not been established. Perhaps the most widely accepted view is that it is a hyper-sensitivity reaction and the fact that it may follow recognised infections,[29] drug intoxications,[40] and serum sickness[32] or may arise spontaneously suggests that the causes are diverse, perhaps a diversity of antigens to which there is a special sensitivity, but a common antigen-antibody response. Since the histological picture of polyarteritis nodosa can be produced experimentally by techniques designed to simulate the "alarm reaction," adrenal cortical activity may be of some importance[14, 35] It is probable that the usual responsible antigen is bacterial in nature because of the relative frequency of preceding infections, especially streptococcal.[29] In this respect the disease resembles rheumatic fever and glomerulonephritis, conditions with which it has been known to be associated.

Clinical features —Polyarteritis nodosa is a disease affecting young adults, 50 per cent. of whom are in the fourth and fifth decades of life. It is four to five times more common in the male than in the female. In these two respects it differs from non-specific granulomatous arteritis and disseminated lupus erythematosus Although a number of cases have been reported in coloured patients it is overwhelmingly a disease of the white race[12]

There is no satisfactory classification of the disease according to combination of clinical findings. In fact the multiplicity of signs and symptoms, more than forty of which have been documented in a wide variety of combinations, is the most constant feature of the disease.[22] It may be confused with any systemic debilitating disease, most frequently tuberculosis, subacute bacterial endocarditis or carcinoma, and if the visceral lesions are localised predomin-

have been detected and verrucose endocarditis may also occur. It is changes such as these and the occurrence of skin eruptions similar to those of disseminated lupus erythematosus that suggest a close relationship between polyarteritis nodosa and the whole group of "diffuse collagen diseases."

Prognosis.—There seems to be little doubt that the prognosis in polyarteritis nodosa is not so grave as originally thought.[24, 36, 38] Almost universally fatal in the acute fulminating types, in the more chronic types the mortality rate is less than 50 per cent. As more mild cases are recognised the case fatality rate will become increasingly lower. Spontaneous remissions and exacerbations interrupt the course of the more chronic types of polyarteritis nodosa. Indeed recovery may be complete. Autopsy, performed on subjects known to have had polyarteritis nodosa, after their death from some other cause, has sometime revealed no residual arterial lesions In the final analysis the prognosis depends upon the site and severity of the disease so that a mild attack in a vital organ, *i.e.* kidney, may lead to death whereas a more acute attack in a non-vital organ, *i.e.* muscle, may be followed by recovery. When death does occur it is usually from congestive heart failure associated with hypertension and renal damage.[34, 36]

Treatment.—There is no specific treatment available for polyarteritis nodosa, but the use of A.C.T.H. and cortisone have been promising.[36] Sulfonamides and antibiotics are of no value. General supportive measures, including blood transfusions, will add to the comfort of the patient.

DISSEMINATED LUPUS ERYTHEMATOSUS

This is a generalised disease of the small blood vessels which is associated with cutaneous eruptions that begin on the exposed surfaces of the body. The aetiology is unknown. It is generally stated that the syndrome is an allergic response to bacterial [illegible] of
a tul [illegible]
eryth [illegible]
cons [illegible] the only
that, [illegible] It seems probable
[illegible] a variety of antigens may be responsible for the pathological picture but certain clinical features permit disseminated lupus erythematosus to be separated as a clinical entity. It is three to four times more common in women, and the peak incidence is in the third decade of life Between 9 and 25 per cent. of patients in reported series are coloured.[19]

Clinical features.—Although the cutaneous eruptions characterise this disease they may be overshadowed and preceded by constitutional symptoms over periods of from a few weeks to several months In the acute cases (disseminated type) the constitutional [illegible]

[illegible] "discoid" stems from the

by hyaline degeneration. This is followed by the second or inflammatory stage in which all the vascular coats are infiltrated with polymorphonuclear leucocytes, lymphocytes, plasma cells and a variable number of eosinophils. This inflammatory reaction extends out into the perivascular connective tissue in varying degrees. The third stage, that of granulation, follows, with fibroblastic proliferation, swelling and further destruction of the internal elastic lamina occurring. Total or partial occlusion of the arterial lumen results and thrombosis is not uncommon. The final stage, that of healing or fibrosis, usually completes the vascular occlusion so that the vessel wall is replaced by scar tissue and perivascular fibrosis surrounds the artery. There may be later recanalisation of the thrombosed vessels



FIG. 280
Polyarteritis nodosa in an arteriole of the small intestine
(*Dible and Davie's Pathology*)

These changes lead to disorganisation and weakening of the vessel wall so that aneurysmal dilatations may form and it is these that can be felt as subcutaneous nodules or seen as circular haemorrhages in parenchymatous organs. The vascular obliteration leads to infarction, necrosis and later fibrosis of the organ in which the disease process is centred. It is these changes that cause the clinical manifestations of the disease, *i.e.* haematuria and albuminuria are due to renal damage, and polyneuritis to an ischaemia of the nerves occasioned by obliteration of their nutrient arteries. Short of autopsy the diagnosis may be made by excision of a subcutaneous nodule or by muscle biopsy, but since muscle is involved in only about 30 per cent of cases a negative muscle biopsy does not exclude the disease.[12]

In a number of cases the kidneys have shown the associated lesions of an acute glomerulonephritis [12, 31] In the heart, lesions similar to Aschoff bodies





A FIG 282 B

Cutaneous lesions on the face (A) and hands (B) of a girl suffering from systemic lupus erythematosus This patient died after ten years of illness (*Patient of Dr. Stephen Gold*)




FIG 283

Hands of pat[illegible]
acu[illegible]

well-defined, circular cutaneous lesions so characteristic of the chronic type of lupus (Fig. 281). Fatigue, fever, tachycardia, weakness, loss of weight and myalgias are common. Gastro-intestinal symptoms may be so severe that surgical exploration may be undertaken on a mistaken diagnosis of acute appendicitis, acute cholecystitis or perforated peptic ulcer. Renal involvement is frequent with albuminuria and haematuria but hypertension rarely occurs Hypochromic anaemia and an elevated sedimentation rate are constant findings.



FIG. 281
Discoid lupus of the face showing chronic, scaly patches and scarring. This woman was sensitive to light (*Patient of Dr. Stephen Gold.*)

The cutaneous lesions may be generalised or localised but usually begin on the exposed surfaces of the body, the hands being commonly affected (Figs. 282B and 283), and the face, where the butterfly distribution is classical (Fig. 282A). Starting as an indefinite erythema of the face it spreads rapidly to the neck, thorax and extremities, becomes reddish violet in colour, scales and fades out With involution the skin may become variably pigmented and so resemble the skin in Addison's disease, scleroderma or dermatomyositis The cutaneous eruption may remain localised, chiefly to the face, or it may be generalised from the outset. About one-third of the disseminated or generalised lesions arise from a pre-existing localised or " discoid " type. The stimuli to

both and in the Libman-Sacks syndrome there may be cutaneous lesions indistinguishable from those in disseminated lupus erythematosus. The former presents a verrucose endocarditis without Aschoff bodies and negative blood cultures However, a verrucose endocarditis is not infrequent in disseminated lupus erythematosus and similar blood vessel changes in the kidneys can be observed in both diseases. Thus it is best to consider the two conditions as manifestations of the same syndrome in which the emphasis has been differently placed

DERMATOMYOSITIS

This is a widespread vascular disease affecting the smaller arteries chiefly of the skeletal muscles of the limbs. Sexes are about equally affected, the middle-aged and children being especially susceptible. The aetiology is quite unknown and all bacteriological investigations have been negative.[11]

Clinical features.—The onset is usually insidious with constitutional prodromata—weakness, malaise, anorexia and weight loss. The diagnostic triad of oedema, dermatitis and myaesthenia then appears, any one of the three *predominating* The skin eruption may be widespread and of variable configuration, resembling that of disseminated lupus erythematosus closely in many instances, and fading to leave the skin deeply pigmented. A frequent and highly [illegible] of the upp [illegible] to involve [illegible] striking pa [illegible] descriptive term—"alabaster face" The cutaneous man[illegible] are [illegible] scles [illegible] the [illegible] involved muscles are found to be atrophied, fibrosed and the seat of contractures. Antecedent or associated Raynaud's phenomenon is not infrequent

Variable pyrexia with a disproportionate tachycardia is common. Leucocytosis is usual and about 20 per cent of patients show an eosinophilia. Albuminuria and haematuria may be found but are not constant.

Pathology.—The fundamental disturbance is in the small arteries of the muscles which has prompted some authors to term the condition "angiomyositis." In its early phases the pathological changes in the vessels are indistinguishable from those in scleroderma Indeed some authors consider that dermatomyositis and scleroderma are [illegible] oedema [illegible][8] There is [illegible] the vessel [illegible] perivascular [illegible] form of necrotising arteriolitis. The muscles show varying degrees of necrosis in the acute stage with oedema and loss of muscle striations going on to fibrosis in the chronic stage

dissemination are variable, *i.e.* sunlight, trauma, or such drugs as sulfonamides, or dissemination may be apparently spontaneous.

PATHOLOGY.—The characteristic features in disseminated lupus erythematosus are in the small arteries, which show endothelial proliferation, subendothelial oedema and degenerative processes in the walls of the vessels The lumen of the involved artery or arteriole becomes narrowed and there is a tendency to thrombosis. Perivascular haemorrhages may occur and perivascular collections of inflammatory cells are not infrequent. The visceral lesions are most frequently found in the kidneys where hyaline thickening of the glomerular arterioles, glomerular thrombosis and fibrosis can be seen. Lamellar fibrous thickening of the splenic arterioles is a very characteristic finding as is also atrophy of the germ centres of lymph glands. Effusions into the serous cavities and verrucous endocarditis may be present and rarely digital gangrene may develop A characteristic finding, which is highly suggestive, is the presence of Lupus cells which are found in the blood by certain techniques[19, 28] (Fig. 284).



FIG. 284
Lupus cells. × 1000.

PROGNOSIS.—In acute cases the mortality rate is 90 per cent at least and few will live more than five years. In the more chronic types of disseminated lupus erythematosus remissions and exacerbations are common and about 50 per cent. will live five years or more, although most of these will ultimately succumb to the disease. Such an opinion was not held by older dermatologists who held a good prognosis for the " discoid " type.

TREATMENT.—Supportive measures may prolong life and in the chronic type of the disease the avoidance of factors which may precipitate an exacerbation or dissemination, is to be recommended A.C.T.H. and cortisone are on trial in this condition and although their use may be followed by a remission such remissions may occur naturally In many cases the improvement is only temporary. Thus it is too early to assess their place in the management of disseminated lupus erythematosus.[14, 19, 28, 31] Favourable response has followed the use of quinacrine hydro-chloride (atabrine) in the discoid type.[30]

THE LIBMAN-SACKS SYNDROME

There seems to be little doubt that this syndrome is but a variant of disseminated lupus erythematosus[3] Constitutional symptoms are common to

anterior aspects of the legs. The nodules are firm, tender, painful and vary in colour from light pink to purple. The overlying skin is never broken and suppuration does not occur Successive crops usually develop each of which lasts about two weeks before involution is complete. In all, the usual attack lasts from two to six weeks. Constitutional reaction is usually mild unless there is an associated infection when the symptoms of that infection overshadow those of the erythema nodosum. Low grade fever, myalgia, malaise and a sore throat are however not uncommon in erythema nodosum even when no associated infection is detected. Recurrence of the disease is rare since [illegible]

[illegible] sting chiefly of oedema [illegible] atory perivasculitis, the cells being lymphocytes and polymorphonuclear leucocytes. The arterioles and venules in the deeper layers of the corium are most extensively affected. Although endothelial proliferation may be seen it is not a feature of erythema nodosum and suppuration and necrosis are not encountered

Erythema nodosum is a self-limiting disease and no specific treatment can be offered Bed rest, hot foments and the use of salicylates, especially when manifestations of rheumatic fever are present, afford some relief. The use of A C T H and cortisone would seem logical and these agents are now receiving a trial

THROMBOANGIITIS OBLITERANS

This inflammatory arteritis of unknown aetiology is discussed in detail in Chapter XI In its acute and early stages it resembles polyarteritis nodosa and like the latter is considered by many to be an allergic vascular reaction to a variety of antigens Bacterial, Rickettsial and fungus infections and in particular sensitivity to tobacco or *one of its* contained contaminants have been incriminated with variable foundation. Pathologically it is an inflammatory, non-suppurative panarteritis in which luminal thrombosis and giant cell formation are commonly observed Histologically it resembles in some respects non-specific granulomatous arteritis with which it has been compared. However the male predominance, the age of onset, the preference for the vessels of the extremitis and the histological characteristics, namely preservation of the internal elastic lamina even in the fibrotic stage, tend to separate it as a clinical and pathological entity It merits mention here because it is an arteritis and can be considered a member of the diffuse collagen diseases until a definite aetiological agent can be demonstrated

SYPHILITIC ARTERITIS

The cardiovascular system is probably involved in every case of active syphilis, the ascending aorta and the aortic [illegible] tion [illegible]

11

TREATMENT.—Supportive measures are adopted for the comfort of the patient and, should he survive, measures designed to minimise the deformity due to contracture are instituted. The mortality rate at present is about 50 per cent. but the prognosis may become more favourable with the advent of A.C.T.H. and cortisone but they must be used in the acute stage to be of any benefit for once contractures are present only orthopedic measures remain.[28, 37]

SCLERODERMA

Scleroderma is discussed in detail in Chapter XIV but it should be mentioned here because of the similarity of its pathological changes to those of dermatomyositis. Both may be considered as examples of diffuse collagen diseases with the skin lesions in scleroderma taking precedence over the visceral and muscular lesions, which may nevertheless be prominent even in scleroderma. The aetiology is obscure and disputed but endocrinological imbalance and vascular abnormalities have been most frequently blamed, as also has, more acceptably, some as yet unknown factor acting generally on the connective tissue of the body. Women in the fourth and fifth decades of life are affected twice as often as men

The cutaneous changes progress through three stages from one of oedema, to one of induration which blends into the final stage of atrophy of the skin and subcutaneous structures in which the patient becomes "hide-bound." Constitutional symptoms are seldom remarkable but myalgias, weakness and weight loss may be complained of. Raynaud's phenomenon is present in most cases.

Pathologically there are two features—changes in the small arterioles and proliferation of the connective tissue stroma. The small blood vessels show endarteritis of variable degree and perivascular infiltration. The endarteritis may lead to obliteration of the lumen of the vessel and accompanying thrombosis has been described. The cardinal vascular changes in scleroderma and dermatomyositis are nearly identical but the clinical pictures are different because of the different organ emphasis in each.

ERYTHEMA NODOSUM

This is an inflammatory disease of the skin and subcutaneous tissues of the extremities in particular, occurring most frequently in females in the second and third decades of life The aetiology is unknown but, as in many similar conditions, it is considered to be most probably a sensitivity reaction of the connective tissues of the body to a bacterial toxin because the history of a preceding infective process is a common finding. The most frequently associated infection is rheumatic fever but erythema nodosum may occur in association with tuberculosis, syphilis, the exanthemata and also with drug sensitivity, particularly to the sulphonamides and barbiturates.

The clinical picture is fairly characteristic with bilateral, and usually symmetrical, nodules of varying size appearing most frequently on the upper,

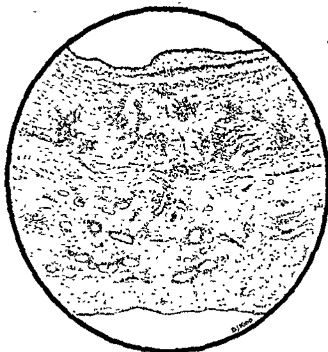


FIG. 285
Syphilitic aortitis in its active phase. (*Dible and Davie's Pathology.*)



FIG. 286
Gummatous periarteritic nodule in the florid stage of syphilis.

a slow, chronic inflammation of the various invaded tissues is progressing Clinically the patient appears in good health and the presence of active syphilis is recognisable only by serological tests. However, in a certain proportion of cases the slow destruction and fibrosis of the involved structures lead to a clinically recognisable breakdown of the cardiovascular or nervous system, although any organ may be affected.

AETIOLOGY AND PATHOLOGY.—The cause of syphilitic arteritis is invasion of the cardiovascular system by the spirochete, treponema pallidum. Symptoms of involvement of the circulatory system seldom become manifest within five years of the primary lesion although the vessels are infected from the beginning. The spirochete becomes distributed in the parts which possess a particularly rich perivascular lymphatic supply and in the cardiovascular system the ascending aorta and the arch of the aorta are most frequently involved. In this respect the distribution is opposite to that seen in atherosclerosis which seldom produces its maximum effects in the thoracic part of the aorta.

Microscopically the middle coat of the aorta bears the brunt of the syphilitic infection. It has been said that the medial lesions are the results of obliterative endarteritis of the vasa vasorum causing a sort of ischaemic atrophy of the muscular and elastic fibres and later aneurysmal dilatation However microscopic examination of the aorta in the florid stage of the lesion shows, in fact, that the middle coat of the vessel is infiltrated with miliary gummatous foci of round cells which, on elastic tissue stain, will be seen to have interrupted the elastic fibres of this part of the aorta (Fig. 285).[8] Accompanying this reaction is a periarterial gummatous inflammation (Fig 286) of the vasa vasorum of the adventitia which have increased greatly in number and which will be seen to extend far into the media to supply the necessary increased blood to the inflammatory infiltrations. It is the healing of the miliary gummata of the media which leads to the characteristic patchy loss of elastic tissue and its replacement by fibrous tissue scars which are so typical of the burnt-out stage of syphilitic mesaortitis.[8] During this healing phase obliterative endarteritis of the vasa vasorum narrows their lumina, such changes accompanying, not causing the changes in the media of the aorta. In the healed stage the elastica is destroyed and replaced by collagenous fibrous tissue so that the aorta loses its resiliency and tends to stretch under the systolic blood pressure and, if the lesion is extensive, aneurysmal dilatation develops

Grossly in the healed stage there is classically a fine wrinkling and puckering of the intima which corresponds to the areas of contraction of underlying fibrous scars of the media. On section the whole vessel is thickened and pale. The intima is hypertrophied and fibrous but this causes little functional damage except when such intimal hypertrophy involves the openings of the coronary arteries. Syphilis rarely, if ever, directly involves the coronary arteries but the aortitis may cause secondary coronary heart disease by occluding the ostia of the vessels.

Clinical features.—Cardiovascular syphilis may manifest itself clinically in one of three ways or it may be a chance finding at autopsy. Most frequently it causes aortic regurgitation with cardiac enlargement.

The next most frequent complication of the destructive mesaortitis is aneurysm formation in the arch or ascending part of the aorta. Such aneurysms may occur in other arteries as well and are discussed fully in Chapter XV. Briefly, here, leutic arteritis and aortic aneurysms are diseases of the middle-aged man being about five times more common in men than women with the peak of incidence in the fifth decade. Fluoroscopy reveals a pulsating tumour in the line of the aorta. Substernal pain may be partly due to the inflammation of the aorta but it is usually due to compression of surrounding structures and bone erosion. The Wassermann or Kahn reaction is usually positive. Least frequently, coronary artery occlusion may follow secondary stenosis of the ostia of the coronary arteries due to the intimal hypertrophy and scarring of the aorta in the region of the sinuses of Valsalva. This with aortic regurgitation may cause angina pectoris.

Syphilitic involvement of the peripheral arteries is rare today but when it does occur in larger arteries like the femoral or popliteal, aneurysm formation results.[25] Less frequent clinical manifestations of peripheral luetic endarteritis, in which the smaller arteries are obliterated, are the symmetrical digital gangrene seen in congenital syphilis of the newborn and a similar symmetrical digital gangrene occasionally occurring in the middle-aged male with acquired syphilis. In the latter individual the digital endarteritis resembles the distal type of thrombo-angiitis obliterans and is felt by some actually to be thrombo-angiitis in a subject who coincidentally has a positive Wassermann reaction. There seems to be little doubt that specific endarteritis can exist though it is becoming exceedingly rare.

The treatment of cardiovascular syphilis is on the whole [illegible]

[illegible] the stage of a developed aneurysm, rupture and fatal haemorrhage can be prevented for from five to ten years. If the aneurysm is localised it is possible to excise it with or without the use of a preserved aortic graft to replace the diseased segment.[2, 25]

TAKAYASU'S DISEASE

In 1908 Takayasu described a disease in which there was thrombosis of one or more of the arteries arising from the aortic arch. The syndrome is almost exclusively found in Japanese females between the ages of twenty and forty years; of the thirty-three cases reported in the literature up to 1951,[30] only three were males and none were Occidental. Lately a number of cases

The mesaortitis with destruction of the elastic fibres and muscle of medial coat of the aorta is the serious feature of syphilis of the aorta. A sin change may involve other arteries as well but is much less common (*Fig. 2* The results of these changes in the aorta are two in the main—aortic inc petence and aneurysm formation. Aortic regurgitation *is by far the commo* complication of cardiovascular syphilis. This is due to dilatation of the a ring and ascending aorta as well as to extension of the infection into

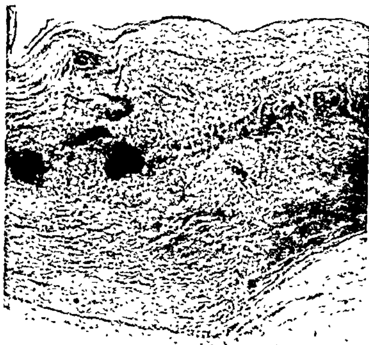


Fig. 287
Florid stage of syphilis in the common carotid artery of a Bantu showing gummatous infiltration of the wall with areas of caseous necrosis and break up of structures
(Courtesy of Dr. C. V. Harrison.)

bases of the valve cusps which become shortened and sclerosed. This combi tion of factors results in the cusps no longer meeting properly and diasto regurgitation into the left ventricle ensues. Cardiac dilatation and hyp trophy, and eventually left heart failure occur. Such a combination of lesio is pathognomonic of syphilitic aortitis and is associated with a diffuse dila tion of the ascending aorta. Aneurysm may arise as a fusiform exaggerati of this process or, more commonly, by the dilatation of a local area in t aortic wall where the loss of elastic tissue and fibrous scarring is particula marked. Once a saccular bulge of this nature is formed it tends to increa in a vicious circle, its walls being formed largely by false fibrous tissue accrui from the pressure atrophy of the tissues on which it impinges. In this wa a large saccular aneurysm may be found with a relatively small opening in the aortic lumen.

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Wasserm [illegible]
can exist [illegible] becoming exceedingly rare.

The treatment of cardio [illegible]
The [illegible]
laxis [illegible] will prevent or at least minimise the complications of the tertiary stage. If untreated the patient with a luetic aneurysm of the aorta will survive about two years after the diagnosis is made If treated adequately even at the stage of a developed aneurysm, rupture and fatal haemorrhage *can be prevented* for from five to ten years. If the aneurysm is localised it is possible to excise it with or without the use of a preserved aortic graft to replace the diseased segment.[2, 25]

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have been reported in the white race and the terms Pulseless disease[41, 44] and Martorell's Syndrome[42] have been suggested. There seems to be little doubt that the more recent reports, particularly those of Martorell[43] and Frovig,[45] are merely variants of the condition first described by Takayasu whose name should be retained eponymously, if any is.

The clinical features of Takayasu's disease depend upon the vessel or vessels obliterated. Only one subclavian artery or one carotid artery may be affected, but in severe cases all of the major arteries arising from the aortic arch are involved. Briefly, the signs and symptoms are those of impaired cerebral and peripheral circulation and may be grouped under three headings. First, pulses are absent in the arteries arising from the aortic arch. Thus the subclavian, axillary, radial, ulnar and carotid arteries may be absent alone or in combination. This leads to weakness and paraesthesiae of the arms and hands but, peculiarly, only rarely do trophic disturbances develop. Secondly, visual disturbances are encountered next in frequency. Examination of the eyes usually reveals arterio-venous anastomoses in the retina around the papilla and in severe disease optic atrophy and cataracts develop. These changes are secondary to obliteration of the carotid artery. Thirdly, the patient may present with a history of orthostatic syncope, dizziness, or epileptiform attacks due to cerebral ischaemia and hypersensitivity of the carotid sinus Such attacks can often be reproduced by pressure on the carotid sinus by the finger or by extending the neck. Less frequently facial atrophy, cranio-cervical pain and intermittent claudication of the muscles of mastication may be present

The aetiology of the condition is unknown and the pathology is obscure. Vascular thrombosis secondary to a panarteritis with disruption of the internal elastic lamina, infiltration of the media and adventitia with lymphocytes, plasma cells and, in some places, granulomatous tissue with giant cells has been reported.[43, 46] This is similar to giant cell arteritis,[43] thromboangiitis obliterans,[47] syphilis and tuberculosis with all of which it has been compared Tubercle bacilli have never been cultured and the clinical features and sex are quite different from Buerger's disease Martorell believes that the condition is the result of atheroma of the arterial openings at their origin from the arch of the aorta.[45]

The results of treatment are disappointing. Cataracts may be removed but this rarely helps the vision. Thromboendarterectomy of a localised obliteration and excision and vein graft have been practised with doubtful benefit. Carotid sinus denervation combined with cervico-dorsal sympathectomy is the procedure of choice The ultimate prognosis is poor with death in months or years usually from progressive cerebral ischaemia.

MISCELLANEOUS ARTERITIS

Arteritis due to specific infection, apart from syphilis, is rare Tuberculous arteritis has been reported[30] but in the vast majority of cases the vascular invasion in tuberculosis is due to local involvement of the blood vessel by

an adjacent granulomatous lesion. Ordinarily a blood vessel is most resistant to external suppuration but an artery passing through a pyogenic abscess may become involved in a panarteritis which weakens the wall. Similar local involvement from without may occur in an actinomycotic abscess or from within by a mycotic embolus from a vegetative endocarditis. Arterial inflammations in these situations usually cause aneurysm formation or rupture of the affected vessel. Indeed this was a common occurrence in the days before asepsis and led to "secondary haemorrhage."

A proliferative, necrotising arteritis with thrombosis of larger arteries and distal gangrene is not infrequent in acute rickettsial diseases (Rocky Mountain Spotted fever) and typhus fever. The picture is similar to that of the acute arteritis of thrombo-angiitis obliterans and has led some authors to consider that the latter is due to a rickettsial infection Generally speaking, however, arteritis due to pyogenic or specific infections, other than syphilis, is rare and of limited clinical importance.

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CHAPTER XIV

RAYNAUD'S PHENOMENON

THE occurrence of intermittent colour changes in the digits is an exceedingly common phenomenon in clinical practice; it may be of little significance or of profound importance. It is necessary therefore to have a knowledge of the condition, some understanding of its mechanism, and an appreciation of its possible consequences

In 1862 Maurice Raynaud[1] published a thesis on "Local Asphyxia and Symmetrical Gangrene of the Extremites" Two types were described, one in which the digits were subject to attacks of "syncope and asphyxia" brought on by cold or sometimes emotion, and another in which symmetrical gangrene of the skin occurred at the tips of cold, cyanotic, painful digits. Later he maintained that the two conditions were merely different stages of the same disease. In all Raynaud described thirty-one cases, and stressed the intermittency of colour changes, the symmetry of incidence and generally the absence of demonstrable arterial occlusion, although in some of the cases which proceeded to gangrene he found permanent occlusion of the smaller vessels due in his opinion to prolonged spasm.

Raynaud drew attention to a common condition, and the series of events in digits so affected became known as Raynaud's disease. He probably did not realise, or at least he did not make it clear, that the intermittent colour change in the digits which he observed and described was merely symptomatic of a number of different conditions, and in fact probably only one of the thirty-one cases in his thesis might now be afforded the title of Raynaud's disease

Jonathan Hutchinson[2] realised the significance of Raynaud's thesis, and appreciated the confusion of cases therein As a result he suggested the term "Raynaud's phenomenon" to indicate intermittent attacks of colour change in the digits occurring in many different disorders, reserving the term "Raynaud's disease" for those cases not associated with other conditions. Hutchinson's paper was largely unnoticed for forty years, during which many cases of digital gangrene were considered as examples of Raynaud's disease, and described as such in the literature, which remained confused.

If the phenomenon as understood by Hutchinson is recognised generally as a symptom of many varied disorders, confusion gives place to order, and since the papers of Lewis and Pickering[3] there has been recognised a distinct disease, characterised by intermittency and symmetry of incidence, with no evidence of diminution or loss of the pulse in major vessels such as those at the wrist or ankle, and with gangrene or nutritional lesions, if any, limited to

the skin. For this condition the eponymous title "Raynaud's disease" is fitting.

Many writers have suggested the abandonment of the terms "Raynaud's phenomenon, and Raynaud's disease" as being unscientific and not descriptive, but no satisfactory alternative name has been suggested, and it seems that apart from the fact that use has familiarised the term with the syndrome, Raynaud's name should be honoured by its retention.

Lewis and Pickering[3] describe the phenomenon as "the active and intermittent closure of small arteries of the order of digital arteries supplying the extremities."

Hunt[4] in an excellent review of the subject suggested a more descriptive definition, viz.:—"Intermittent pallor or cyanosis of the extremities precipitated by exposure to cold, without clinical evidence of blockage of the large peripheral vessels and with nutritional lesions, if present at all, limited to the skin." While this is a clinical definition, it excludes those occasional cases in which there is an associated major vessel occlusion, as occurs in atherosclerosis occasionally and thromboangiitis more frequently, and we prefer a more liberal definition—" Intermittent attacks of pallor or cyanosis, or both, occurring in the extremities, on exposure to cold."

Clinically the condition consists of *intermittent attacks* of pallor or cyanosis, or of pallor followed by cyanosis, occurring as a result of cold or rarely of emotion.[5] In the earlier stages one or two of the finger tips only may be affected; but as the disease advances so the effect is seen in the other digits and even in the distal part of the palm. The thumbs are rarely affected. This is due to the fact that the blood supply to the thumb is relatively greater than is the blood supply to the other digits, and also that the thumb is shorter with less surface area per unit volume than the other digits, and therefore less active in response to changes in temperature. For the same reason the toes are rarely affected.

The degree of cold required to induce an attack varies with the stage of the disease. At first a digital temperature of 18°C. is needed to precipitate the phenomenon, whereas in more advanced cases a temperature of 25°C. will be sufficient. The body temperature is of almost more importance, and it is impossible in early cases to induce an attack in a patient who is thoroughly warmed,[4] although some observers do not agree with this.[6] We have been able in advanced cases with proven obliterative disease of the digital arteries to induce spasm by the application of local cold to a digit, the patient's body being warmed, but we have not been able to produce the spasm in such circumstances unless there has been evidence of some degree of organic narrowing or obliteration of these vessels. The presence or absence of narrowing or obstruction of the digital arteries in some part of their course would account for the varied reports with regard to this particular problem. However, if the whole body is chilly, simply grasping a cold object, or putting the hand or foot in the region of a draught will precipitate an attack. In the male, where

Raynaud's phenomenon is often a symptom of thromboangiitis obliterans, the attacks come on frequently whilst shaving in the mornings when the body temperature is low, and when the fingers are subjected to reduction of temperature by the evaporation of moisture from the hands.

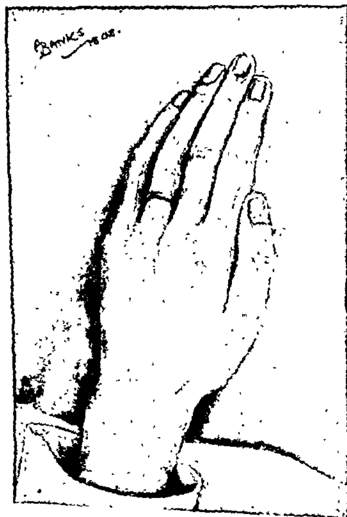


FIG 288

Secondary Raynaud's phenomenon in a hand ... asting of finger ... re present In ... ction, and this

Whether pallor or cyanosis occurs first seems to vary from case to case, and also in the same patient according to the position and function of the hand at the time If the hand is below the level of the heart, and at rest, cyanosis occurs, and this may be of any degree—" my hands go black " is commonly

the skin. For this condition the eponymous title "Raynaud's disease" is fitting.

Many writers have suggested the abandonment of the terms "Raynaud's phenomenon, and Raynaud's disease" as being unscientific and not descriptive, but no satisfactory alternative name has been suggested, and it seems that apart from the fact that use has familiarised the term with the syndrome, Raynaud's name should be honoured by its retention.

Lewis and Pickering[7] describe the phenomenon as "the active and intermittent closure of small arteries of the order of digital arteries supplying the extremities."

Hunt[4] in an excellent review of the subject suggested a more descriptive definition, viz.:—"Intermittent pallor or cyanosis of the extremities precipitated by exposure to cold, without clinical evidence of blockage of the large peripheral vessels and with nutritional lesions, if present at all, limited to the skin." While this is a clinical definition, it excludes those occasional cases in which there is an associated major vessel occlusion, as occurs in atherosclerosis occasionally and thromboangiitis more frequently, and we prefer a more liberal definition—"Intermittent attacks of pallor or cyanosis, or both, occurring in the extremities, on exposure to cold."

Clinically the condition consists of intermittent attacks of pallor or cyanosis, or of pallor followed by cyanosis, occurring as a result of cold or rarely of emotion.[5] In the earlier stages one or two of the finger tips only may be affected; but as the disease advances so the effect is seen in the other digits and even in the distal part of the palm. The thumbs are rarely affected. This is due to the fact that the blood supply to the thumb is relatively greater than is the blood supply to the other digits, and also that the thumb is shorter with less surface area per unit volume than the other digits, and therefore less active in response to changes in temperature. For the same reason the toes are rarely affected.

The degree of cold required to induce an attack varies with the stage of the disease. At first a digital temperature of 18°C. is needed to precipitate the phenomenon, whereas in more advanced cases a temperature of 25°C. will be sufficient. The body temperature is of almost more importance, and it is impossible in early cases to induce an attack in a patient who is thoroughly warmed,[4] although some observers do not agree with this.[6] We have been able in advanced cases with proven obliterative disease of the digital arteries to induce spasm by the application of local cold to a digit, the patient's body being warmed, but we have not been able to produce the spasm in such circumstances unless there has been evidence of some degree of organic narrowing or obliteration of these vessels The presence or absence of narrowing or obstruction of the digital arteries in some part of their course would account for the varied reports with regard to this particular problem. However, if the whole body is chilly, simply grasping a cold object, or putting the hand or foot in the region of a draught will precipitate an attack. In the male, where

rapidly deoxygenated by tissues rendered anoxic by a period of complete ischaemia In mild cases the affected parts recover if they are warmed; in severe cases, if the whole body is chilled, it too must be warmed. A hot drink, or alcohol, often relieves an attack, just as it warms up normal extremities that have been chilled (Figs 288 and 289).



FIG. 290
Skin atrophy, paronychial infection and ridging of the nails are seen



FIG. 291
Terminal scars of healed gangrenous ulcers are seen.

Advanced cases can only keep comfortable by remaining in an overheated atmosphere, and we have recently seen a woman with Raynaud's phenomenon who spent the day in front of an open gas oven door, by no other means could she maintain circulation in her fingers. A similar case has been reported by White and Smithwick.[7] Sufferers from the condition rarely get an attack when the body is really warm, as for example when warmed by exercise on a cold day, even if the hands are uncovered. In mild cases an attack can be stopped by rubbing the hands, warming them by the fire, or by immersion in warm

stated. If the hands are in active use or above the level of the heart, pallor is more common at the onset. Pallor is usually, but not necessarily always, fol-



FIG. 289
The arteriogram of the hand depicted in Figure 288 There is marked distal arterial obstruction

lowed by cyanosis before recovery occurs, and the cyanosis again may change to pallor if the attack is prolonged. *Cyanosis in these circumstances* is due to small amounts of blood flowing through relaxing digital vessels and becoming



Fig 293

CLASSIFICATION OF CONDITIONS IN WHICH RAYNAUD'S PHENOMENON APPEARS

I PRIMARY RAYNAUD'S PHENOMENON *or* hereditary cold fingers, in which there is no organic occlusion of arteries.

II SECONDARY RAYNAUD'S PHENOMENON, in which there is probably always some organic narrowing or occlusion of vessels. It occurs after:—

A Trauma . .	1 COLD. 2 ISOLATED INJURY. 3 CONSTANTLY REPEATED INJURY. 4 VIBRATION INJURY
B Collagen diseases . . .	1 SCLERODERMA. 2 DISSEMINATED LUPUS ERYTHEMATOSUS. 3 RHEUMATIC FEVER AND RHEUMATOID ARTHRITIS. 4 PERIARTERITIS NODOSA. 5 DERMATOMYOSITIS

water. Recovery takes place from the base of the finger and spreads to the tip of the finger, and often individual fingers recover independantly. A rather bright brick red colour spreads up the finger slowly, replacing the cyanosed or pale area; this is a reactive hyperaemia, which persists for several minutes until the fingers regain their normal colour.



FIG. 292
Rather extensive cutaneous digital gangrene occurring in a woman of 53 years The arteriogram (Fig 293) shows extensive obstruction of the digital arteries

Sensory changes accompany the vasomotor changes. Early in the attack the fingers become numb, clumsy and stiff, and are often the site of a severe ache. If the attack is prolonged there is nearly always some detectable diminution of sensation—epicritic sensation disappearing before deep sensation, as would be expected. During the period of recovery there is tingling, " pins and needles," and often a burning sensation for a few minutes—symptoms which may be quite distressing.

Raynaud's *phenomenon*, in the absence of narrowing or obstruction of the arteries, may persist throughout life, without significant increases in severity and with no trophic changes in the digits. On the other hand, when it is associated with vascular disease, it may within a year or two of onset proceed to nutritional lesions involving the skin and subcutaneous tissues. The finger pads atrophy giving a tapered appearance to the digit, which is often shiny as a result of disappearance of the normal corrugations of the skin. Paronychial infections are common (Fig. 290); the nails become brittle, ridged, and irregular in growth and they may fail to grow Small painful gangrenous ulcers may occur on the finger tips, but at first these generally heal in warmer weather, leaving depressed scars (Figs 291-293), in some cases the ulcers penetrate to the bone carrying infection to it with atrophy and absorption Bone atrophy occurring in severe cases in the absence of penetrating ulcers is probably due largely to disuse of the digits It is not common (Fig. 127).

Raynaud's phenomenon occurs most commonly in the fingers, but may also occur in the toes, nose and ears, has been seen in the tongue,[7, 8] and has even been reported in the retina when it is associated with blurring of vision[9]

The above clinical description applies to Raynaud's phenomenon and its sequelae, and it may occur in a large number of different conditions

Emotion, such as shyness, fear and anxiety, is sometimes an aetiological factor in precipitating an attack. Although the condition may be troublesome and annoying, it is not complicated by permanent changes in the skin and subcutaneous tissues, and the digits are normal between attacks and in a warm atmosphere Primary Raynaud's phenomenon frequently occurs in association with acrocyanosis, erythrocyanosis and perniosis. Cracks and fissures are sometimes seen, particularly in cold weather. Sometimes after a whitlow they [illegible]

arterial disease, or "Raynaud's disease," when it might appear that the primary phenomenon had in fact progressed to trophic change. Alternatively, a patient suffering from "Raynaud's disease," for example, *may* give a history of a Raynaud's phenomenon from childhood with perhaps further evidence of an unstable peripheral circulation such as chilblains, whereas patients with secondary Raynaud's phenomenon and "Raynaud's disease" do not usually afford such a history. The extreme frequency of primary Raynaud's phenomenon explains its common coincidence with other disorders.

As Raynaud remarked, hereditary cold fingers are due to "local syncope *in its simplest form*" and the patient can be reassured that there is no risk of complications subsequently occurring

SECONDARY RAYNAUD PHENOMENON

This may occur as a result of.—

A. Trauma.—1. COLD.—Hunt[4] subjected himself to a prolonged experiment in a cold bath and found that he could not induce vascular stasis in his extremities until he had reduced his body temperature to below 95°F. Richards[6] noticed his fingers to be cold and bloodless on removing his gloves when climbing a mountain on a very cold day. In both cases a typical Raynaud's phenomenon developed *in the fingers*, but there was no development of recurrent attacks on exposure to lesser degrees of cold. Learmonth[10] reported the case of an airman who *flew without* gloves at a high altitude, but *in his* case the attacks were occurring four years later on exposure to *moderate* cold at ground level. Richards[6] also has reported the cases of men whose attacks have *persisted after single* exposures to severe cold.

In some cases therefore *a single attack* of Raynaud's phenomenon may be induced by exposure to cold, *especially if the* body temperature is low. Severe cold, however, may give rise to a *permanent* tendency to attacks of complete vascular stasis, but it *is probable* that this only occurs if the cold is of such intensity to *damage* irreparably the vessels of the digits, so that it is really a mild degree of frostbite In the chronic stage of frostbite, and as the result of "immersion foot," a Raynaud's phenomenon is a frequent symptom and *results* from endarteritis of vessels subjected to severe or persistent cold

C. **Nervous disorders**	1 [illegible] 2. [illegible] cic
D. **Obliterative vascular disease**	1. ATHEROSCLEROSIS. 2 THROMBOANGIITIS OBLITERANS. 3 ARTERIAL EMBOLISM AND THROMBOSIS 4. *In cervical rib and superior thoracic outlet syndromes.*
E. **Stasis in the smallest vessels**	1. SYPHILITIC ARTERITIS. 2. HAEMAGGLUTINATION. 3. IN SOME SEVERE GENERAL ILLNESS SUCH AS: (*a*) LEUKAEMIA. (*b*) POLYCYTHAEMIA. (*c*) ADVANCED PULMONARY TUBERCULOSIS. (*d*) MALARIA.
F. **Certain intoxications**	1. ERGOT POISONING. 2. HEAVY METAL POISONING, E G. LEAD AND ARSENIC.

III. RAYNAUD'S DISEASE.—This, if an entity apart from scleroderma or other collagen disease, is always associated with organic narrowing or occlusion of the digital arteries.

PRIMARY RAYNAUD'S PHENOMENON OR HEREDITARY COLD FINGERS

This is by far the commonest cause of Raynaud's phenomenon, seen in both sexes, but more frequently in females. It affects the fingers more often than the toes and is usually but not always symmetrical Amongst the nursing staff of one small hospital twenty-eight out of seventy-two nurses complained of some degree of pale or cold fingers, or poor circulation—but in only two had the spasms become more frequent or more severe in the last five years. Although commonly starting at the age of seven or eight, it may also appear for the first time at a much later age, in the second or third decade; and there is almost always a history of the condition in other members of the same family. In childhood many of both sexes suffer from cold fingers or toes, especially when bathing on a cool day, but there is a tendency for attacks to become less frequent and less severe as the years pass. At puberty and again at the menopause there appears to be a tendency for the attacks to disappear. On the other hand, especially when the disease starts in later life in the second or third decade it may persist, or even get worse over the course of years from the normal ageing of the digital arteries as expressed by thickening of the intima It never progresses to trophic changes, such as wasting of the finger pads or skin atrophy, and when the body and the extremities are warm, the fingers are completely normal, and digital artery pulsations can be felt. Elderly people may be seen, in their sixth and seventh decades, who have complained of " bad circulation " and frequent attacks of vasospasm for fifty years or more yet in whom there is no trophic change or wasting whatsoever.

Emotion, such as shyness, fear and anxiety, is sometimes an aetiological factor in precipitating an attack. Although the condition may be troublesome and annoying, it is not complicated by permanent changes in the skin and subcutaneous tissues, and the digits are normal between attacks and in a warm atmosphere. Primary Raynaud's phenomenon frequently occurs in association with acrocyanosis, erythrocyanosis and perniosis Cracks and fissures are sometimes seen, particularly in cold weather. Sometimes after a whitlow they will heal and not recur in the affected finger.

It may of course happen that a sufferer from primary Raynaud's phenomenon may develop another condition such as a collagen disease, obliterative arterial disease, or "Raynaud's disease," when it might appear that the primary ... Alternatively, a patient ... give a history of a Ra ... rther evidence of an unstable peripheral circulation such as chilblains, whereas patients with secondary Raynaud's phenomenon and "Raynaud's disease" do not usually afford such a history. The extreme frequency of primary Raynaud's phenomenon explains its common coincidence with other disorders.

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In some cases therefore a single attack of Raynaud's phenomenon may be induced by exposure to cold, especially if the body temperature is low. Severe cold, however, may give rise to a permanent tendency to attacks of complete vascular stasis; but it is probable that this only occurs if the cold is of such intensity to damage irreparably the vessels of the digits, so that it is really a mild degree of frostbite In the *chronic* stage of frostbite, and as the result of "immersion foot," a Raynaud's phenomenon is a frequent symptom and results from endarteritis of vessels subjected to severe or persistent cold

2. INJURY.—A Raynaud's phenomenon localised to a digit injured by violence or infection rarely occurs. It has been reported following injury by a fives ball; we have seen it after incision of a whitlow, after an incised wound of the base of the digit and after a linear electric burn of the distal inter-phalangeal creases of the index and middle fingers of the left hand In this patient the phenomenon was strictly limited to one side of the phalanges distal to the burn, which had been sustained as the result of grasping a high tension wire. In all these examples, it is probable that there is some underlying vascular injury resulting in narrowing or obstruction of the lumen of the digital vessels.

A man aged fifty-four years complained of a Raynaud phenomenon in the tip of the third left finger. Ten years previously he had suffered an incised wound over the antero-lateral aspect of the finger at the level of the distal inter-phalangeal joint, from which time Raynaud's phenomenon had been present and limited to the digit distal to the scar of the wound. From the position of the wound it appeared probable that the digital artery at the site had been severed

The phenomenon has also been reported after fractured clavicle, sprain of the wrist joint, crushing and bruising injuries or gunshot injuries in the region of large blood vessels and complicating oedema in limbs the site of previous fractures. We have recently seen a case involving the thumb, index and middle fingers in a woman of sixty-seven following a fractured scaphoid. It has been suggested that involvement of main vessels or nerves by scar tissue may have some bearing on the development of the phenomenon distally.[11]

Sudeck's atrophy (p. 575).—Raynaud's phenomenon is sometimes, but not always, seen in cases of Sudeck's atrophy or painful osteoporosis. Sudeck's atrophy is a condition arising as a result of trauma or inflammation in the region of a joint, particularly the wrist or ankle, and may also occur after a simple surgical operation at this site. In addition to patchy osteoporosis apparent radiologically, there is pain, tenderness and swelling in the region of the joint and for some distance distally, and a cyanotic, moist and cold skin Movement of the joint is avoided, owing to the pain produced, thus leading to further interference with function and vascular changes resulting from disuse In addition to these, phasic colour changes may be superadded. Leriche[12] described the vascular changes and stressed their importance, and pointed out that, following the early hyperaemic phase at the injured site, Raynaud's phenomenon appeared in the chronic phase.

3. CONSTANTLY REPEATED INJURY.—The repeated minor trauma of the digits occurring in pianists and typists leads occasionally to the occurrence of Raynaud's phenomenon in the fingers most in use. The symptoms may be quite disabling, necessitating in some cases avoidance of the occupation or recreation.

4 VIBRATION INJURY OR PNEUMATIC HAMMER DISEASE.—Manual workers using vibrating tools or pneumatic hammers are liable to acquire a Raynaud's phenomenon in one or both hands.[13] The attacks may start after using the tool for periods of six months and occur most commonly with a vibration rate of 2,000 to 3,000 per minute, particularly where hard metals are being machined Thus it has been reported that sixty-one out of seventy-two workmen were affected when hard metal was being worked, as against sixteen out of thirty-one working with soft metal.[14] "Hot riveters" are not affected to the same extent as are "cold riveters," the hot metal being softer. The common occupations involved are stonebreakers, riveters, caulkers, fettlers, drillers and shoemakers, whereas scalers, grinders, holders-up and rivet cutters are rarely affected, the vibration rates of the tools used in these latter occupations being 6,000 or more or 1,000 or less per minute. The pneumatic hammers are held in right-handed men with the right hand and balanced on the middle, ring and little fingers of the left hand, the tool being guided by the index and thumb of the left hand. It is the supporting digits of the left hand which are subjected to the greatest vibration, and it is in these that the attacks first start. It is interesting to note that these fingers are nearest the working end of the tool which becomes hot after use, and the right hand holding the rear trigger-end is often icy cold as a result of its proximity to the escape of compressed air. This suggests that temperature is not a factor in production of the syndrome. Owing to the weight of the heavier tools the hands may be changed round, when the corresponding fingers of the other hand will often become affected The thumbs if subjected to vibration are the site of spasm, an unusual site in other varieties of Raynaud's phenomenon The vasospastic attacks are typical, and may be severe with eventual gangrene,[15] although this is rare but more common after the age of fifty years[16] Cold causes the attacks of vasospasm and they generally persist even if use of the tool is given up, but they may occasionally recover after a year or more The digital nerves may also suffer as a result of the [illegible] as the fingers may [illegible]

In the lesser [illegible] and workers tend [illegible] job, but if it progresses a change of occupation should be advised

B. Collagen diseases.—The collagen diseases[18] are a group of conditions which have a similar underlying basic pathology consisting of fibrinoid degeneration of collagen tissue Some of these diseases appear to be of allergic origin, and all that can be said at the present time is that they exhibit the result of reaction to some form of injury of the connective fibroblastic tissues of the body Amongst the fibrous tissue affected is frequently that of the blood vessels leading to medial sclerosis often associated with intimal proliferation and resultant narrowing and obstruction of the vessel lumen These diseases in their active phase show a raised erythrocyte sedi-

mentation rate and sometimes a reversal of the albumin-globulin ratio. Those collagen diseases in which a Raynaud phenomenon is seen are:—

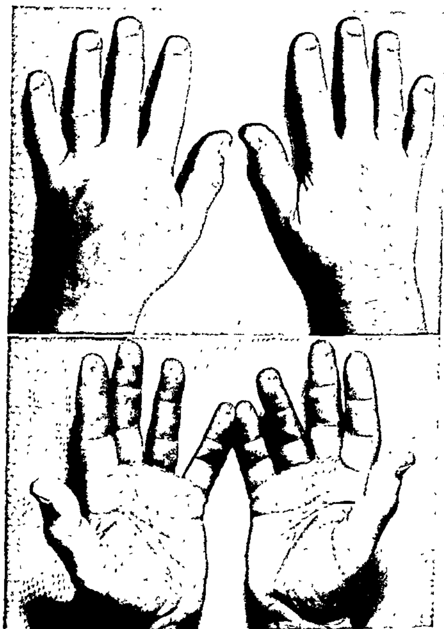


FIG. 294

Scleroderma There is marked atrophy of the digital skin, thickening of subcutaneous tissues and limitation of movements of the fingers The patient, a man of fifty-seven years, suffered severe attacks of Raynaud's phenomenon.

1. Scleroderma
2. Disseminated lupus erythematosus
3. Dermato-myositis
4. Periarteritis nodosa.
5. Rheumatoid arthritis and rheumatic fever.



FIG. 295

Marked calcium deposits in the periarticular tissues of the knee joint in a child.

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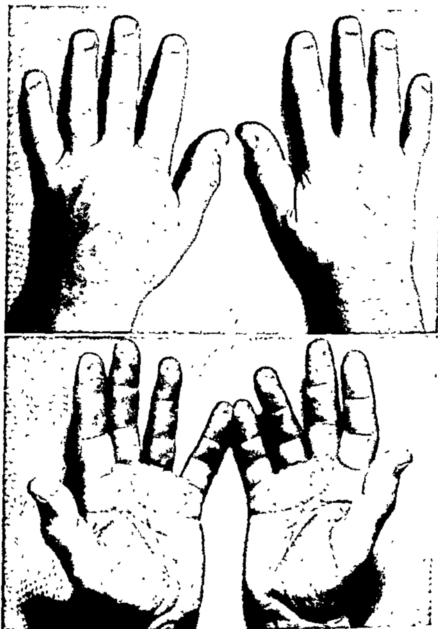


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2. Disseminated lupus erythematosus
3 Dermato-myositis
4. Periarteritis nodosa.
5. Rheumatoid arthritis and rheumatic fever.

there is an associated Raynaud's phenomenon which tends to become severe as the vascular changes advance. Later trophic changes in the digits are common The vascular changes may be present up to five years before the ... of the skin of the fingers becomes evident, although in such cases ... limitation of flexion ... kin and ... nce and vascular symptoms are usually but not always ... in degree. Calcinosis or deposits of calcium phosphates in the subcutaneous tissues of the digits and in the periarticular tissues is sometimes seen, and there may be absorption of bone of the terminal phalanges (Figs. 295 and 296).



FIG. 297
Section of a finger amputated for gangrene due to scleroderma Complete obstruction of the digital vessels is seen

Ulceration and phlyctenular gangrene are frequent and massive gangrene of a whole digit is not uncommon (Fig. 297). Progress of the condition in the hands leads to interference with the grip and to inability to pick up small objects, the fingers being swollen, clumsy and numb from persistent ischaemia, and there is loss of the normal skin corrugations. The skin of the face is sometimes thickened and this usually follows the digital changes (Fig. 298). At first there is a sensation of stiffness, and later the skin loses its creases and wrinkles and becomes smooth, shiny and immobile, and the lips become stiff and their *movements restricted* Involvement of the nose and ears, with rarely a superadded Raynaud's phenomenon, may occur. In addition to fibrosis of the skin, periarticular fibrosis and visceral manifestations of the disease frequently occur (Fig 299). Fibrosis of the gastro-intestinal tract, especially of the oesophagus, and the lungs, heart and kidneys, is seen in varying degrees and

1. SCLERODERMA.—This is a well recognised condition characterised by dense sclerosis of the skin and subcutaneous tissues of the fingers, hands,



FIG 296
Severe bone absorption occurring in a patient with scleroderma Calcinosis is also apparent on the ulnar side of the radio-carpal joint

forehead, ears, bridge of nose, neck, shoulders and upper part of the back and front of the thorax. The thighs are sometimes affected, the feet rarely The skin changes may be limited to the hands, and in about half the cases

A female aged forty-four was seen complaining of intermittent discoloration and numbness of the left index finger. This had occurred for the first time after a motor car accident two weeks previous. She had received no apparent injury but she had been very disturbed mentally.

At the time of examination the left index finger was cold and cyanosed. The middle finger and little finger of the left hand and the index and ring fingers of the right hand were also affected but less so than the left index Both index fingers felt stiff and there was slight swelling and some limitation of flexion.

Bilateral sympathectomy of the second and third thora...

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Ten months later she reported again with occasional spasm and cyanosis of the left index and right fourth fingers, but there was no evidence of sympathetic activity in either hand All the digits showed limitations of flexion as a result of thickening and fibrosis of their skin

Three years after operation she returned with a small patch of gangrene at the tip of the left fifth finger and recurrent Raynaud's phenomenon of all fingers except the third and fourth of the right hand. The thumbs were not affected. There was evidence of some ret...

"Priscol" in

she remained

all the fingers

Five year ... operation the vascular phenomena in the fingers remained in the same state as two years previously, but there was increase in the fibrosis of the skin of all the digits except the right third and fourth digits and wasting of the tips of the affected fingers with skin atrophy. She was taking "Priscol" in the colder weather but not in the warmer months At this time there was a definite sclerosis with thickening and loss of wrinkles over the bridge of the nose and the forehead, a condition typical of scleroderma She had no chest symptoms, no dysphagia and was otherwise well

The original sympathectomy markedly improved the circulation in the left index finger, although within a year there was deterioration, and at this time there was involvement of other fingers. Three years after operation return of sympathetic function led to further circulatory embarrassment with the onset of phlyctenular gangrene. This was relieved by "Priscol." It was not until five years after the onset of the Raynaud's phenomenon that involvement of the facial skin confirmed the diagnosis of scleroderma

Treatment.—A large number of drugs, hormones and vitamins have been used in the treatment of this condition, few if any with effect Some improvement may be obtained with ACTH but there appears to be complete relapse on withdrawal of the drug [21, 22] Improvement of the digital symptoms may occur following sympathectomy, but in two advanced ...

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... and also in the prevention or at least in delay of

their frequent association has led to the suggestion that "progressive systemic sclerosis" is a more suitable term for this generalised disease.[19, 20]

The clinical picture therefore may be varied; in addition to the digital signs there may be dysphagia, arthritic symptoms, renal symptoms and cardio-respiratory embarrassment. Pigmentation of the skin and spidery naevi, possibly as a result of liver involvement, are often seen. The disease occurs



FIG. 298

There is loss of corrugations in the frontal region, and the lips assume a somewhat "pursed" appearance due to sclerosis of their skin



FIG. 299

Scleroderma of the oesophagus The oesophagus is a rigid tube in its lower part There is no peristalsis This female patient *complained of* Raynaud's phenomenon only.

more commonly in females than males, and we have seen patients so affected between the ages of fifteen and fifty-five years. It may become stationary at any stage, or it may progress rapidly, often with periods of quiescence interspersed with periods of activity, often accompanied by mild pyrexia. Involvement of the internal organs of the body may lead to death from fibrosis and infection of the lung aggravated by constriction of the chest wall by thickened inelastic skin, or myocardial fibrosis or even renal fibrosis Most patients show a raised erythrocyte sedimentation rate during the active phase of the disease, and about half the cases have a hyperglobulinaemia and a reversal of the albumen-globulin ration. Circulation tests of digits subject to Raynaud's phenomenon show evidence of impairment of digital blood flow, and arteriograms of the digital vessels reveal segments of complete vascular obliteration very similar to the appearances seen in distal thromboangiitis obliterans. The occurrence of a Raynaud's phenomenon in such cases is the result of a normal physiological reaction to cold in arteries already narrowed or obstructed

drug Raynaud's phenomenon is sometimes improved. Sympathectomy, owing to the multiplicity of the lesions throughout the body, is not indicated (*see* p 475)

3. DERMATOMYOSITIS.—This is a disease affecting the muscles giving rise to marked tenderness and a profound weakness leading to prostration and sometimes severe dysphagia from involvement of the pharynx and oesophagus. In addition the skin of the arms and legs and other areas is the site of swelling and a bright red rash, and there is associated stiffness of the joints. The disease may be acute or chronic and is accompanied in the acute stages by a severe pyrexia with often a polymorphonuclear leucocytosis[24] Raynaud's phenomenon may occur in the hands Muscle biopsy reveals the diagnosis (*see* p 479).

4. PERIARTERITIS NODOSA —This is a condition first described by Rokitansky[25] occurring usually in males, of any age. It consists of an angiitis affecting any artery or vein in the body and appears to be a hypersensitivity phenomenon. Only short segments of vessels are involved, and aneurysmal dilatations sometimes occur. In half the cases there is a marked eosinophilia ranging from 10 to 70 per cent. or more, though it may be absent in the later stages of the disease. The symptoms are diverse, but there is generally acute or chronic sepsis with fever and anaemia, in addition to neuritic, muscular and abdominal pains. Involvement of renal, gastrointestinal, pancreatic, coronary and cerebral vessels gives rise to symptoms associated with these organs Various skin lesions may occur, and joint pains resembling rheumatic affections are common [illegible] nt of the digital vessels may result in Ray- [illegible] gangrene has been recorded.[26] The eryth- [illegible] The disease is often, but not always, fatal, but cortisone is of value in treatment, and the outlook less gloomy with its use (*see* p. 472)

5 IN ASSOCIATION WITH ACUTE RHEUMATIC INFECTIONS AND RHEUMATOID ARTHRITIS.—Raynaud's phenomenon is not uncommon in association with rheumatic affections and occurs usually in the early stage of the disease, but sometimes later. Sometimes after a few days, intermittency of attacks may be lost, the hands or feet assuming a persistently cold blue appearance at which stage suitable tests may show marked organic occlusion of the peripheral vessels However, after a few weeks there is partial or complete recovery from the occlusive stage, leaving a persistent Raynaud's phenomenon in the former case The changes occur in the fingers and [illegible]

[illegible] and tender or stiff joints. Nodules in the flexor tendons are frequently present, and the E.S R. is persistently raised in the active stages of the disease It is interesting to note that rheumatic heart disease and periarteritis nodosa are seen not infrequently in association with one another suggesting a basic similarity of their pathology.[27] It is most

their recurrence. When there is gross digital artery obliteration sympathectomy will achieve little as arterial obstruction may be so extensive that local cold alone will be sufficient to produce complete vascular occlusion. The disease process is unaffected by the operation and will proceed in its normal course, unless, as indeed often occurs, it becomes spontaneously arrested. In only a few patients have we been convinced that sympathectomy has had any important and reasonably prolonged effect. We therefore perform the operation only where the vascular symptoms are not excessively severe, where sclerosis of the skin is not marked and where there is no evidence of disease in the internal organs. If immersion of the affected hand in cold water induces vascular stasis, the rest of the body being warmed, sympathectomy will be of no benefit.



FIG. 300
Lupus cells. × 1,000

2. DISSEMINATED LUPUS ERYTHEMATOSIS.—This is a disease occurring almost exclusively in women and characterised by a prolonged pyrexial illness with rheumatic pains and associated with confluent red eruptions occurring on the exposed parts. The parts affected are the bridge of the nose, cheeks, ears and the upper part of the chest, and there are frequently associated telangiectases The skin lesions are often initiated by exposure to sunlight There is no sclerosis of the skin nor of the gastrointestinal tract. Involvement of the digital arteries results in narrowing and obstruction of their lumina and a consequent Raynaud's phenomenon. There may also be erythematous macules on the tips of the fingers and toes and over the palms and soles

Leucopenia, microscopic haematuria, polyserositis, nephritis and vascular [illegible] the absence of any syphilitic infection, the blood Wassermann reaction is [illegible] positive. Lupus cells (Fig. 300) are usually found in the venous blood or bone marrow during the active phase of the disease, but their presence is not confined to this condition.

The disease may pursue a prolonged course over years and is accompanied by exacerbations often with cardiac and pulmonary complications, and it is frequently but not always eventually fatal

Treatment.—Cortisone in large doses is usually effective in the acute exacerbations of the disease but the treatment is not without some danger. However, the more acute the disease, the more effective is treatment with this

digits become tapered and lose their corrugations, and the finger pads waste. The joints become stiff from fibrosis of the periarticular tissues, and the bone of the digits decalcified. Chilblains appear in the subcutaneous tissues and may ulcerate, and wounds and abrasions are slow to heal. All these signs and symptoms are evidence of disuse and there is no vasomotor disorder, nor is there any vascular obliterative process, although there may be atrophy and luminal narrowing of the vessels themselves Swelling of the limb may occur as a result of malnutrition of capillaries resulting from prolonged ischaemia with alterations in their permeability. The circulation therefore in a paralysed limb does not exhibit the changes typical of a Raynaud's phenomenon, but in so far as the vessels in such cases are capable of reflex vasodilatation, colour changes are intermittent and might be considered examples of this phenomenon.

CERVICAL RIB.—Vascular symptoms complicating a cervical rib or thoracic outlet syndrome occur occasionally. A cervical rib detected on X-ray examination is by no means necessary evidence that the symptoms are caused by the rib. In fact vascular complications of cervical rib are distinctly uncommon

The most usual complication is a progressive cyanosis of the hand with nutritional lesions or even gangrene in the fingers. There is often diminution or absence of the major pulses, but in a small proportion of cases there is, for a short time in the course of the disease, a true Raynaud's phenomenon, but the intermittency of vasospastic attacks tends soon to give place to permanent cyanosis, the condition thus merging into the more common type associated with major arterial obstruction. Diagnosis is assisted by the presence of pain in the neck, shoulder girdle and over the deltoid, together with shooting pain down the arm to the hand, often severe, and there may be paraesthesiae in the fingers. Nerve symptoms may, however. be absent [illegible] dilatation of [illegible] heard over this reg[illegible] particularly in the [illegible] fingers.

The mechanism of the vascular symptoms associated with cervical rib is discussed in Chapter XVIII.

D. Obliterative arterial disease.—Raynaud's phenomenon occurs in a small proportion of cases of atherosclerosis The incidence is generally not symmetrical and is usually associated with evidence of major arterial obstruction in the limbs The onset is generally after the age of forty-five and the attacks of pallor or cyanosis are more prolonged than in other forms. Rarely the attacks may be symmetrical rendering clinical diagnosis difficult, but oscillometry, plethysmography, and occasionally arteriography will assist. Loss of a major pulse will make the diagnosis probable and evidence of intimal calcification in the greater vessels will be added evidence. In the feet the pallid phase may recover only on prolonged heating of the body.

In thromboangiitis obliterans a Raynaud's phenomenon in the fingers, often of one hand at first, and occasionally in the toes, may be the first indica-

important to recognise these rheumatic cases, as a sympathectomy performed during the course of active rheumatic disease may be followed by pericardial effusion.[17] If sympathectomy is performed, this should be done after the rheumatic element has become inactive as shown clinically, and by a normal erythrocyte sedimentation rate (Fig. 301).

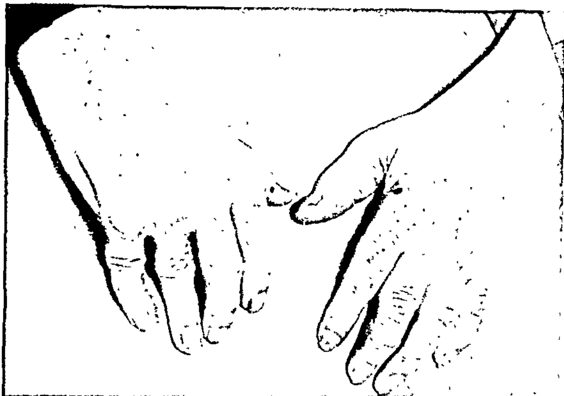


FIG. 301
Severe rheumatoid arthritis These hands were subject to attacks of Raynaud's phenomenon Paronychia and phlyctenular gangrene can be seen.

C. Nervous diseases.—In those diseases and disorders of the nervous or locomotor system, which result in paralysis a disuse atrophy occurs in the paralysed part. A normal person who keeps one hand hanging by his side for an hour, using or exercising the other hand, will find that at the end of that time the idle hand is cooler than its active fellow It is also slightly cyanosed Activity of a hand or foot increases its blood supply, whereas one at complete rest requires only minimal blood supply. If a limb as the result of paralysis of motor nerves, or of muscles, remains inactive for a prolonged period, a condition commonly seen in anterior poliomyelitis, gross wasting of the structures occur, although there is no interference with the vasomotor supply of the vessels of that limb. In a cool room the affected limb will be found to be cooler and cyanosed, but when the patient's body is heated complete vasodilatation can be procured, the vessels of the limb dilating fully and completely. Nevertheless full vasodilatation is an infrequent state for such a limb and it suffers from prolonged anoxia resulting in chronic cyanosis and atrophy The

Haemolysis, probably a purely local phenomenon, also occurs in the presence of cold, when oxyhaemoglobin and probably methaemoglobin and methaem-albumin may be detected in the blood, and this destruction of red cells is, no doubt, the origin of the anaemia present in patients with this complaint. Haemoglobinuria can sometimes be detected, but not always so as haemolysis may be minimal

Clinically the condition occurs in either sex and the first symptom is cyanosis of exposed parts, especially of the fingers in the presence of cold. On re-warming the part, the circulation returns to normal. Stasis from obstruc-



FIG. 302
Digital gangrene from high-titre cold agglutinins.
(*By Courtesy of Dr S Nelson*)

tion of the capillaries by agglutination can be recognised by the fact that local pressure on the cyanosed finger will not cause blanching, whereas it will do so in Raynaud's phenomenon from other causes (Parisius phenomenon). The whole hand may be affected, as it is not in the majority of patients with Raynaud's phenomenon in whom only the digits are involved. Later there may be trophic changes in the skin of the fingers with loss of sensation, and after prolonged exposure to cold, gangrene, which is usually symmetrical (Fig 302). Arterial pulses are normally palpable at the wrist.

Anaemia of the haemolytic type may be severe, and the erythrocyte sedimentation rate is considerably raised, sometimes more so at low temperatures,[32] but this is not always the case.[29] The process of agglutination can be observed with a slit lamp corneal microscope occurring within conjunctival vessels on instilling a drop of ice cold water into the anaesthetised conjunctival sac.[33]

Treatment.—Treatment is unsatisfactory. Cold should be avoided by the use of gloves or mittens, and cold metals should not be handled. Vasodilator drugs and sympathectomy are ineffective, as would be expected, for stasis is the result of arterial obstruction and there is no evidence of any vasospastic element in the disease.[28] No success has followed efforts to prevent

tion of the disease in a proportion of cases. It is considerably more commor during some period in the course of this disease than it is in atherosclerosis Other evidence of thromboangiitis, such as *recurring superficial thrombo phlebitis* or obliteration of a vessel elsewhere in the limbs may be present although such evidence may not be forthcoming for a period even of years A first the phasic colour changes may not be accompanied by clinical evidence o arterial obstruction, but we have found that distal vessel obstruction can alway be demonstrated by arteriography. When the changes occur for the first time ir a man in his second, third or fourth decade, the eventual development o thromboangiitis is exceedingly probable unless there is some other reason fo the phenomenon such as vibration injury or collagen disease.

OBSTRUCTION OF A MAJOR VESSEL at the root of the limb, may give rise to a Raynaud's phenomenon in the digits. In such cases the greatly diminished flow in the digital vessels can be completely arrested by the normal reaction of the body and the part to cold.[17]

A woman aged twenty-four, as a result of an operation at the root of the neck, suffered division of the subclavian artery. She complained of a severe Raynaud's phenomenon involving all four fingers, but not the thumb, in addition to intermittent claudication in the forearm and hand muscles.

THROMBOSIS OR EMBOLISM of a more proximal vessel results on occasions in a distal Raynaud's phenomenon. Thrombosis in the femoro-popliteal vessel is sometimes followed by pallor and coldness in the toes which is only relieved by the patient sitting in front of a fire or taking a hot bath.

E. In association with stasis in the small vessels—1. SYPHILIS.—Raynaud's phenomenon occurs sometimes in congenitally syphilitic infants, and there is often an associated haemoglobinuria. Hunt[4] has emphasised an association between Raynaud's phenomenon and syphilis with necrosis in the nose and ears of adults.

2. HAEMAGGLUTINATION —Patients whose serum contains cold agglutinins in high titre are liable to attacks of cyanosis or Raynaud's phenomenon of the exposed parts—fingers, ears, nose or other exposed skin. Occasionally otherwise normal persons suffer, but it occurs more commonly as a complication or virus pneumonia and more rarely in association with haemolytic anaemia, cirrhosis of the liver and trypanosomiasis, when it may be present only for a short time during the height of the disease. In the otherwise normal person high titre cold agglutinins may appear in the blood rather suddenly, and once they appear they tend to persist.

The syndrome has recently been fully discussed by Nelson and Marshall (1953).[29] As a result of cold from 0°C. to 10°C. or to a less extent from 10°C. to 20°C. agglutination of the red cells occurs in the cooled parts On re-warming the agglutination disappears and the circulation returns to normal In any particular case, if cold is sufficiently prolonged, thrombosis may occur and then the condition becomes irreversible, and gangrene may result[30, 31, 29]

It does not seem, therefore, that intoxications by heavy metals have a direct aetiological significance in Raynaud's phenomenon.

"RAYNAUD'S DISEASE"

"Raynaud's disease" has many features in common with scleroderma. It first appears between the ages of twenty-five to forty-five and affects women, rarely men Although in the earliest cases clinically indistinguishable from primary Raynaud's phenomenon or hereditary cold fingers, it is a rapidly progressive condition, and sometimes severe from the onset. The attacks of discoloration and circulatory arrest are soon prolonged, and in the intervals between the attacks the tip of one or more fingers may not recover circulation fully for a considerable time after the patient is thoroughly warmed, even after lying in a hot bath Trophic changes occur early. Atrophy of the skin, irregularity or cessation of nail growth, persistent paronychia, wasting of the finger pads and often rarefaction of the terminal phalanges soon appear. In a large proportion of cases small necrotic areas appear at the tips of the fingers, and these may be excruciatingly painful. They slowly separate leaving small depressed scars, but the ulcers tend to recur, leading eventually to shortening of the terminal phalanges, not only from loss of soft tissue but also from bone absorption. Massive gangrene of a finger is rare, but has been recorded occasionally.[40, 6]

There is a remarkable symmetry shown in the digits affected, for example, the middle and index fingers of each hand may be first attacked soon to be followed by perhaps the tip of each ring finger. The disease progresses until all the fingers, rarely the thumb, become affected symmetrically both as regards distribution and severity; the patient becomes miserable and apprehensive as the spasms become more frequent and prolonged, and the circulation is relatively normal for only occasional periods of the day. It is said that the nose and ears are not affected, and calcinosis does not occur. Although the hands are predominantly affected, the disease is also seen occasionally in the toes. Although commoner in women, we have under our care two men with signs and symptoms which fulfil all the clinical criteria (p. 516). A previous history of chilblains or Raynaud's phenomenon in childhood, or in other members in the same family, is not part of the condition but does not preclude the diagnosis Excessive sweating has been described as a frequent occurrence[41] but it is, in our experience, uncommon.

In patients with Raynaud's phenomenon and trophic changes in the digits, a normal blood fl[illegible]
heral
that
[illegible] studies always show that the maximum blood-flow is below the normal level and arteriography will demonstrate some degree of organic arterial occlusion of the digital vessels in these circumstances In primary Raynaud's phenomenon, in which trophic change does not occur, there is never any evidence of organic obstruction of the digital

the formation or inactivation of the agglutinins once they are present. ATCH has been without effect.

A similar tendency to clumping or to "tangling" of sickle cells within the lumen of the small vessels apparently occurs in haemoglobin C disease, a condition seen almost exclusively in negroes. In the presence of cyanosis, sickle cells appear in the blood, and these may aggregate to such an extent that interference with the normal blood flow occurs, and symptoms of ischaemia. We have seen severe ulcerating and gangrenous chilblains in a *female Jamaican patient with sickle cell haemoglobin C disease, and the* unusual severity of the condition in this instance may well be due to aggravation of the local ischaemia from clumping of the excessive numbers of sickle cells, themselves increased in number from the cyanosis usual with chilblains.[34]

3. IN SOME SEVERE GENERAL ILLNESS such as polycythaemia vera, *leukaemia*, advanced pulmonary tuberculosis and *malaria. In these conditions* Raynaud's phenomenon occurs late in the course of the disease the mechanism being one of intravascular agglutination of red cells similar to that which occurs in cold haemagglutination, and there is close association between haemagglutination and a high erythrocyte sedimentation rate.[4]

F. Certain intoxications—1. ERGOT POISONING.—Lewis[35] found that injections of preparations of ergot in the cock caused vascular changes in the comb. A single injection caused spasm of the arteries which persisted for thirty-six to forty-eight hours, with damage to the endothelium and thrombosis.

In epidemic ergot poisoning not only are there vascular signs but also *neurological manifestations such as psychological changes*, paraesthesia of heat and cold, muscular twitchings and occasionally convulsions. The vascular signs are usually persistent cyanosis or gangrene. Raynaud's phenomenon has been reported following the use of ergot preparations *medicinally*,[36] but in spite of the very frequent use of ergotamine tartrate for migraine, such symptoms are very rare The use of this drug for pruritus associated with jaundice has been complicated by vasospastic attacks on a number of occasions.[37, 38] We have not encountered a case of Raynaud's phenomenon which could be attributed to ergot intoxication

2 HEAVY METALS.—For many years intoxication by heavy metals has been considered responsible for the occasional incidence of Raynaud's phenomenon, but we are not aware of any particular instance *where this has* been the case. Atherosclerosis may result from lead poisoning and this may give rise to vasospastic attacks in the digits, but then the Raynaud's phenomenon results not from any action of lead on the vessels, but *rather* from atherosclerosis Sensitisation to mercury is a possible factor in the aetiology of Pink disease in children,[39] but the colour changes in the condition are not intermittent, and are therefore not examples of Raynaud's phenomena.

In 1929 Lewis, as the result of prolonged investigation and the most detailed observations, criticised the theory of sympathetic overactivity and concluded that the attacks of vasospasm were due to some local fault in the digital arteries resulting in their hypersensitivity to cold. This theory was based on the following observations:—

1 Local cooling of the base of a finger will produce an attack, even if the rest of the body is warmed to such an extent that reflex vasodilatation occurs.

2 A peripheral nerve block by local anaesthesia will not always relieve an established spasm.

3 Sympathectomy does not always relieve the spasms, and even if it does, there is a strong tendency for the condition to relapse.

Lewis made his observations on patients with severe disease but arteriography has shown that such patients have organic arterial disease, and this fact has considerable influence on the interpretation of his findings. We have found it possible to induce an attack in an isolated hand, the rest of the body being warmed, only in those patients whose digital vessels are the site of marked organic obstruction, and in similar cases an established spasm can only be relieved by peripheral nerve block if the hand is warm

Apart from the circulation within the blood stream of chemical substances or hormones which may influence the distal blood-flow there are two factors largely concerned in the production of spasm in the digital vessels, supplying as they do a large surface area by means of which temperature regulation of the body is controlled These are central sympathetic nervous action and local temperature of the part Now unusual central sympathetic activity in certain circumstances can produce as a response to bodily cold peripheral vasoconstriction of such a degree as to lead to a typical Raynaud's phenomenon in persons who have never previously suffered from it. This occurs frequently after extensive removal of the thoraco-lumbar sympathetic trunk in operation for hypertension, when it might be assumed that the remaining upper thoracic trunk exhibits excessive activity in an attempt to maintain body temperature Local cooling of the digit of a normal person results in marked diminution of blood flow (Figs. 303 and 304) [illegible]
in normal [illegible]

[illegible] phenomenon, but they can
[illegible] the body temperature and the [illegible]

[illegible] and normally encountered
[illegible] cold is not surprising and is seen frequently; in fact, it is the most usually encountered variety of the Raynaud's phenomenon and appears to be the mechanism in primary Raynaud's phenomenon or hereditary cold

arteries, even after the condition has been present for many years. T
"Raynaud's disease" appears to be an obliterative arterial disease, affe
digital arteries. Hyndman and Wolkin[42] after a review of the available
have also concluded that "Raynaud's disease" is primarily a vascular

Many patients with "Raynaud's disease" followed for some ye
eventually developed stiffness and thickening of the digital skin altho
may not occur until years have passed. Lewis remarked: "A number
patients (*with* Raynaud's disease), *and especially those in whom t*
dition comes rapidly, develop diffuse scleroderma." Such cases
believe, examples of scleroderma, where a Raynaud's phenomenon h
dated often by years the changes in the skin.

"Raynaud's disease" has been thought to be associated with en
changes.[17] Raynaud considered there was a relation between the sev
the symptoms and the menopause, as in his opinion the only well-
exciting cause was a suppression of the menses, and "as a count
he had seen a notable amelioration or indeed a complete cure coinci
the re-establishment of this function."

Whether "Raynaud's disease" is an entity apart from sclerode
not, trophic changes occur soon, sometimes a few months after the o
the phenomenon, and if the patient with Raynaud's phenomenon do
develop trophic change after two years, then his symptoms are attril
to primary Raynaud's phenomenon or non-progressive conditions ass
with trauma. Those patients with an increasingly severe Raynaud's
menon and trophic changes who do not develop sclerodermatous char
the digital skin can be considered to be examples of Raynaud's disea
it must be confessed that it is difficult to say that they are not examp
scleroderma which have stopped short of producing sclerosis in the s
elsewhere.

Aetiology of Raynaud's Phenomenon

Raynaud considered that the vasospastic attacks resulted from ar
active sympathetic nervous system, although he offered no explanatio
this came about. This theory remained unchallenged for fifty-five yea
appeared to be confirmed by the finding that sympathectomy was fol
almost invariably by some improvement, and often cure of the con
especially in the milder cases.[43, 44] Changes in the sympathetic ganglia
been described and include oedema, infiltration with lymphocytes
degeneration, and have been held responsible, in some way, for sympa
overactivity,[40] but similar changes have been found at post-mortem exa
tions in subjects dying from other causes[45] with no history of Rayr
phenomenon, and therefore such changes do not appear significant. I
been shown recently that recurrence of symptoms following sympathec
operations bears a very close relationship to the recovery of sympa
function.[46, 47]

loss of subcutaneous fat in the fingerpads Blood examination, serology, and the erythrocyte sedimentation rate were normal There were no ischaemic symptoms in the feet and no history of thrombophlebitis He had never worked with vibrating tools A bilateral sympathectomy was done by the anterior approach and the con-



FIG. 305

Patient with Raynaud's phenomenon Primary vascular disease of the digital arteries Good filling of the palmar arch and some of the palmar veins but a number of digital arteries, second, third and fourth fingers, are thrombosed close to their origin

dition
with gr
patheti
305)

A
nerves ... approach was made and the ...

fingers. Munro[19] stated that in this condition "local syncope is the result not of a normal physiological process, but of the exaggeration of a normal process." In primary Raynaud's phenomenon, which may occur for the first time not only in the first decade but in the second and third decades, there are no trophic changes even after the condition has persisted forty or fifty years. The circulation returns to complete normality between attacks, and

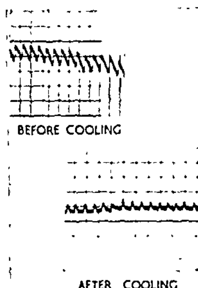


Fig. 303

Oscillometric recordings in the terminal phalanx before and after local cooling of the digit.

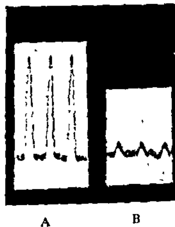


Fig. 304

Oscillometric recordings in the terminal phalanx with the body warmed (A), and with the body cooled (B), the temperature of the digits being maintained at an even temperature. These variations are due to sympathetic activity.

the attacks themselves are readily and rapidly relieved by either local or bodily warmth—in other words if one of the two factors necessary for their production is removed. We have tried to induce a spasm in digits affected by primary Raynaud's phenomenon in the presence of ulnar nerve block but have been unable to do so, and furthermore an established attack can be relieved by immersing the affected hand in warm water, the remainder of the body being cold.

If the blood-flow to the digits is interfered with by intimal thickening or obstruction, either of the digital vessels themselves or of the larger vessels in the limb, then the two factors of local cold and central sympathetic activity very much more readily produce Raynaud's phenomenon, and as the obliterative element advances, so one factor alone may be sufficient to induce complete stasis of blood-flow in a digit.

A male, aged forty-five, was first seen in April, 1952, complaining of severe Raynaud's phenomenon of all the fingers of both hands, the right hand being affected more so than the left. The attacks first occurred the previous winter whenever he was out of doors, and were accompanied by stiffness and numbness of the digits. The pulses at the wrist were normal and full, the skin was atrophic and there was

but some cases of digital gangrene have been reported. Further, such tests as have been used to estimate the presence or absence of any narrowing or obstruction have all depended on digital temperature recordings, a method distinctly unreliable in the detection of minor alterations in blood-flow. As it is only the digits affected by the vibration which are the site of the phenomenon, we cannot escape the conclusion that the repeated insults of vibration to the digital arteries leads to a reaction in these arteries, expressed by intimal thickening or obstruction, probably from bruising of the vessel walls.

A quarry worker, aged forty-two years, presented with gangrene of the terminal phalanx of the right middle finger. There had been a Raynaud's phenomenon of gradual onset in the second, third and fourth fingers of the right hand, over the previous seven months. The affected fingers had been exposed to vibration from a pneumatic drill, and there was no evidence of ischaemia elsewhere, and no history of thrombophlebitis.

A cervical sympathectomy was done, and the gangrenous finger amputated through the middle phalanx. It was noted at the time of amputation that there was no bleeding from the divided digital arteries.

Section through the terminal phalanx revealed considerable intimal thickening of the arteries, certainly abnormal in degree (Fig. 306). It seems that the main brunt of the vibration, when using tools of this type, falls on the proximal phalanx. It might be that as a result of this the digital arteries at this level became occluded by thrombosis—there was no bleeding from these at operation. The intimal thickening of the arteries at the level of the terminal phalanx might result from lesser degrees of trauma or from a diminished blood flow through them as a result of proximal occlusion.



FIG. 306

Gross intimal thickening in the digital artery of a finger amputated for gangrene. The base of the finger had been subjected to vibration injury. The section is through the terminal phalanx.

(By Courtesy of Mr. H. S. Shucksmith.)

If therefore these conceptions of the aetiology be accepted, the discrepancies between Lewis's observations and those of other observers can be explained. In severe Raynaud's phenomenon from whatever cause, if there is digital artery obstruction, local cold alone will in some cases produce an attack, even if sympathetic control is abolished by peripheral nerve block or reflex heating. In lesser degrees of disease, we have never failed to relieve an established spasm by peripheral nerve block, but in an advanced case, with gross disease of the arteries, it may only be by excessive local warmth as well that return of circulation to a digit so affected can be achieved.

all the tissue and pleura overlying the necks of these second and third ribs removed Following this procedure there was no detectable sympathetic function in the hand, but the attacks of vasospasm were unaltered in severity and could be induced on cooling of the hands. The only way the patient could remain comfortable was by wearing wool-lined leather gloves. In this patient therefore there was gross obstruction to the blood-flow through the digital arteries and local cold alone was sufficient to induce Raynaud's phenomenon.

Simmons and Sheehan[49] reported a few similar cases, and they attributed the stasis to spasm in vessels themselves hypersensitive to cold but they did not publish arteriograms of such cases. It may be that arteriography would have revealed arterial obstruction. In cases of primary Raynaud's phenomenon or hereditary cold fingers Lewis had the opportunity of examining the digital vessels on six occasions and found them to differ in no way from the vessels of unaffected digits of a similar age group. In more severe cases of Raynaud's phenomenon occurring in "Raynaud's disease," however, he found intimal thickening to be marked. Digital artery thrombosis has been noted in such a case, and medial thickening and fibrosis of the intima involving the digital arteries has been reported.[50] It has been shown that the flow in the digits between attacks of spasm is less than it is in normal fingers.[51] Arteriography in cases of "Raynaud's disease," even without evidence of trophic change, showed that the digital arteries of most patients do not appear to be filled normally in their distal parts.[52] It has been suggested that the intimal thickening and subsequent thrombosis in "Raynaud's disease" result from recurrent spasm. If this were so it is surprising that cases of primary Raynaud's phenomenon which have persisted for many years, even fifty or more, are not accompanied by deterioration in the nutrition of the digits and interference with nail growth, both of these evidence of organic narrowing or obstruction. In Raynaud's phenomenon associated with progressive scleroderma and thromboangiitis obliterans severe nutritional change, phlyctenular gangrene and rarely massive gangrene may occur. In these conditions we know from arteriography and from microscopical examination of the digital vessels that there is an obliterative arterial disease present. Raynaud's phenomenon in these circumstances is merely the result of normal physiological action on a vessel through which the circulation is obstructed in some degree.[17] Similarly in some cases of rheumatic affections, there is involvement of the arteries themselves leading to narrowing and even thrombosis and it may be that it is in this variety of affection that attacks of stasis occur

Raynaud's phenomenon occurring after exposure to severe cold and "immersion foot" results from damage to the digital arteries which respond by intimal thickening and sometimes even by intra-vascular thrombosis of varying degree. It also occurs if bruising or laceration has resulted in interruption of the vessel lumen. As regards its occurrence after vibration injury, the evidence in regard to any direct damage to vessels is confused.

thickening and sclerosis so that it cannot be "pinched up" from the underlying phalanges, and other evidence, thickening of the facial skin and visceral changes may be present If the phenomenon occurs for the first time in a woman in the third, fourth or fifth decades, is symmetrical in onset and incidence, and is significantly more severe over the course of two winters, a diagnosis of "Raynaud's disease" can be considered, provided other evidence of collagen disease can be excluded. The distinction between "Raynaud's disease" and scleroderma is often impossible, and the fact remains that many patients with symptoms suggesting the former may ultimately develop the latter disease

In *disseminated lupus erythematosis* the skin is thinned and atrophic, and can be "pinched up" from the phalanges. There is usually a scaly erythema of the skin of the exposed parts of the body, and generally an erythematous blush involving the face. Fever is often present. The disease is very rare in the male

In either sex an early onset coupled with a history of the condition in other members of the family would indicate a *primary Raynaud's phenomenon*, in which there are no trophic changes in the digits, though painful cracks may occur The age of onset is in the first, second or third decades, but the disorder does not progress significantly in severity, is not necessarily symmetrical in incidence, and often affects the toes as well as the hands. Tests of the circulation will reveal no organic arterial obstruction between spasms. Arteriograms always appear normal.

In older persons *atherosclerosis* may be present, and attacks of vasospasm may rarely occur when the vessels at the root of the limb are obstructed, the distal vessels being patent. Calcification, the presence of disease in the lower limbs in those patients whose fingers are affected, opthalmoscopic changes and possibly an associated hypertension will all indicate the diagnosis. Raynaud's phenomenon in the fingers is distinctly uncommon in atherosclerosis.

Swollen joints and a raised blood sedimentation rate suggest a *rheumatic origin* for the phenomenon. A positive Wassermann reaction and other serological tests might indicate a *syphilitic* origin, but by no means necessarily mean that syphilis is the cause. A Raynaud's phenomenon does occur rarely in congenitally syphilitic infants and Hunt[4] draws attention to the fact that invariably when there is necrosis of the nose and ears, and in many cases when there is associated haemoglobinuria, there seems to be a history of syphilitic infection *Cervical rib, or superior thoracic outlet syndrome* infrequently give rise to vasospastic attacks. Cervical rib can be excluded by X-rays, although the presence of a supernumerary rib does not necessarily mean that it is the cause of the symptoms Absence of neurological signs and symptoms will help to exclude conditions arising at the superior thoracic outlet. Other rare conditions such as *cold agglutination*, and *severe systemic diseases* such as leukaemia, polycythaemia rubra vera, malaria and tuberculosis can be

Our conclusions are therefore first, that primary Raynaud's phenomenon —hereditary cold fingers—is an innocuous disease, with a good prognosis and no danger of subsequent trophic change, and is merely an exaggerated local and general physiological response to cold or possibly to emotion, the latter acting via the sympathetic system. Second, the severity of Raynaud's phenomenon associated with obliterative vascular conditions depends on the progress or otherwise of the vascular disease. Third, as suggested by Lewis, it is only in obliterative vascular disease that trophic changes occur in the digits.

" Raynaud's disease " is rare, although Raynaud's phenomenon is very common. " Raynaud's disease " advances in severity, and trophic changes are often found within a few months of the onset of the disease. When present, the clinical condition varies little from that seen in thromboangiitis obliterans or scleroderma where a Raynaud's phenomenon often is the presenting symptom, and its progress towards severe nutritional change is similar Like these two conditions it may remain stationary at any stage in its progress

Diagnosis

A large number of conditions associated with cyanosed and ischaemic hands and feet have been called "Raynaud's disease" The diagnosis of Raynaud's phenomenon depends on intermittency of colour changes, the digits being apparently normal between attacks. Such conditions as acrocyanosis, erythrocyanosis, the cyanosis of *Pink disease* and *incipient gangrene* with persistent colour changes in obliterative vascular diseases are therefore readily excluded.

Having established the presence of Raynaud's phenomenon, its cause must be determined. If there is a history of the use of *vibrating tools*, previous *local injury* of such a nature as to damage the distal vessels, or exposure to unusual and *severe cold*, the diagnosis will be indicated.

Raynaud's phenomenon is an occasional first symptom, and a frequent later symptom, of *thromboangiitis obliterans*. In such patients examination may reveal evidence of peripheral vascular obstruction elsewhere, and there may be a history of recurring superficial thrombophlebitis Sometimes, however, Raynaud's phenomenon involving one or more digits, often in one hand alone, may be the only clinical manifestation of the condition, although arteriography will reveal narrowing or obstruction of the vessels of the affected digit. Thromboangiitis obliterans is practically confined to men. It may be impossible to differentiate thromboangiitis obliterans involving the digital vessels only from scleroderma without prolonged observation of the patient, although in the latter condition there is a tendency for all the digits of the hands to be affected.

" *Raynaud's disease* " and *scleroderma* affect the hands symmetrically, and are considerably less common in men The skin of the digits may show

thickening and sclerosis so that it cannot be "pinched up" from the underlying phalanges, and other evidence, thickening of the facial skin and visceral changes may be present. If the phenomenon occurs for the first time in a woman in the third, fourth or fifth decades, is symmetrical in onset and incidence, and is significantly more severe over the course of two winters, a diagnosis of "Raynaud's disease" can be considered, provided other evidence of collagen disease can be excluded. The distinction between "Raynaud's disease" and scleroderma is often impossible, and the fact remains that many patients with symptoms suggesting the former may ultimately develop the latter disease.

In *disseminated lupus erythematosis* the skin is thinned and atrophic, and can be "pinched up" from the phalanges. There is usually a scaly erythema of the skin of the exposed parts of the body, and generally an erythematous blush involving the face. Fever is often present. The disease is very rare in the male.

In either sex an early onset coupled with a history of the condition in other members of the family would indicate a *primary Raynaud's phenomenon*, in which there are no trophic [illegible] occur. The age of onset is in [illegible] does not progress significant[illegible] incidence, and often affects the toes as well as the hands. Tests of the circulation will reveal no organic arterial obstruction between spasms. Arteriograms always appear normal

In older persons *atherosclerosis* may be present, and attacks of vasospasm may rarely occur when the vessels at the root of the limb are obstructed, the distal vessels being patent. Calcification, the presence of disease in the lower limbs in those patients whose fingers are affected, opthalmoscopic changes and possibly an associated hypertension will all indicate the diagnosis. Raynaud's phenomenon in the fingers is distinctly uncommon in atherosclerosis

Swollen joints and a raised blood sedimentation rate suggest a *rheumatic origin* for the phenomenon. A positive Wassermann reaction and other serological tests might indicate a *syphilitic* origin, but by no means necessarily mean that syphilis is the cause. A Raynaud's phenomenon does occur rarely in congenitally syphilitic infants and Hunt[4] draws attention to the fact that invariably when there is necrosis of the nose and ears, and in many cases when there is associated haemoglobinuria, there seems to be a history of syphilitic infection *Cervical rib, or superior thoracic outlet syndrome* infrequently give rise to vasospastic attacks. Cervical rib can be excluded by X-rays, although the presence of a supernumerary rib does not necessarily mean [illegible] cause of the symptoms. [illegible] to exclude conditions [illegible] Other rare conditions such as *cold* [illegible], and *severe systemic diseases* such as leukaemia, polycythaemia rubra vera, malaria and tuberculosis can be

recognised by examination of the blood or by other manifest signs and symptoms of the more serious conditions present.

Treatment

As cold is the commonest precipitating factor in the occurrence of the Raynaud's phenomenon, treatment should be directed towards its avoidance. Body warmth is as important as local warmth, and suitable warm and windproof clothing should be worn. The hands and feet should be adequately covered in cold weather with suitable mittens, and woollen stockings should be advised.

Warm rooms, avoidance of cold water and a warm bed at nights should be encouraged, points which the patient will have discovered for herself. Work with vibrating instruments should be forbidden as should the handling of cold metals with ungloved hands. As regards drug treatment Priscol appears to be the most useful drug available at present. Priscol or 2-benzyl-4, 5-imidazaline hydrochloride appears to act on the smaller arteries of the hands and feet, and particularly on the skin vessels. Not only has it a paralysing action on the functional tissue of the sympathetic nervous system, but it also acts directly on arteries and neuromuscular junctions.[53, 54, 55, 56] The drug has been used extensively and improvement of cutaneous circulation has been demonstrated in some cases as shown by oscillometry, skin temperature and fluorescein time observations.[57] Clinically many patients showing Raynaud's phenomenon, and especially primary Raynaud's phenomenon, are considerably improved, and some markedly so Furthermore, the clinical effect of Priscol is often particularly marked after sympathectomy, an association which has been noticed in a patient whose symptoms had recurred following a quadrilateral sympathectomy a year previously.[55] A patient has also been reported in whom a single injection of 50 mg. of Priscol produced results lasting for seven days with relief of pain and freedom from spasms during this time.[55]

Priscol should be given in doses of from 25 mg. to 75 mg. three times a day, starting with the smaller dose in order to assess the patient's tolerance Unfortunately there are unpleasant side effects, such as faintness, flushing, dizziness, headache, sweating, nausea, vomiting, " gooseflesh " and " shiver down the spine," and some patients are unable to use the drug. If belladonna is given at the same time, the nausea and vomiting are avoided. There is no doubt that in purely vasospastic conditions Priscol is a drug of great value, if the side effects are not excessive, but its use has to be continued indefinitely Furthermore, after prolonged use its effect tends to wear off. On the other hand by no means every patient responds, for reasons which are not understood. Hunt[58] has been impressed with the results obtained by the use of Ronicol, and he considers it superior to Priscol.

Other drugs such as alcohol, intravenous papaverine, calcium, theobromine, prostigmine and many others do not appear to be of any clinical value.

The nitrites are short acting and cause dilation of vessels of the head and neck before those of the extremities. Nicotinic acid may cause a rise in skin temperature of the extremities and its action is more prolonged than is that of the nitrites but the intense flushing of the face is a trying complication. Carbachol or Emechol ionisation is said to be useful in vasospastic conditions, but we have no experience of this method of treatment.

The fingers must be protected from injury, and any scratch, abrasion or sepsis must be carefully treated Cracks and fissures can be softened by massage with lanoline

SYMPATHECTOMY FOR RAYNAUD'S PHENOMENON

If Raynaud's phenomenon is due to a hyperactive sympathetic nervous system, then interruption of the sympathetic nerve fibres to the part should result in cure. If the phenomenon is due to local cold acting on the vessels, then sympathectomy should not have such a pronounced effect. The fact is that sympathectomy always results in marked vasodilatation of the cutaneous vessels of the digits, but unfortunately there is a marked tendency to relapse. A discussion of the causes of this relapse will indicate to a large extent which patient should be selected for sympathectomy.

There are three theories to account for this tendency to relapse, *viz.*:—

1. Increased sensitivity to circulating adrenalin following sympathectomy.

2 The condition of local vessels, whether showing local sensitivity to cold or, as we believe, some narrowing or obstruction.

3 Recurrence of sympathetic activity.

Clinically there are two distinct types of relapse, that which occurs early during the first week or two following sympathectomy and that which occurs six or more months after operation and gradually increases in severity up to five years when it appears to remain stationary.[40] These two varieties of relapse result from different mechanisms, the first being due to pre-existing arterial obstruction of the digital vessels, and the second to a recurrence of sympathetic activity. Early relapse is rare, but occurs from time to time, and we have seen it on three occasions. The first patient was a doctor's wife aged forty-two with "Raynaud's disease" who had her first spasm of digital vessels before her discharge from hospital on the tenth post-operative day. The other two were in men operated on for Raynaud's phenomenon in association with scleroderma Simmons and Sheehan[40] mention similar cases, one relapsing four days after operation. It might be argued that such early relapses are due to incomplete denervation at operation, but in our cases and in Simmons's cases sympathectomy had been complete.

1. **Increased sensitivity to adrenalin.**—Dale and Richards[9] have shown that in animals the smooth muscle of vessels deprived of their nerve supply is more than usually sensitive to circulating adrenalin. Further it has been claimed that this sensitivity is more marked if the denervation has been carried

out by post-ganglionic section of the nerves, with consequent degeneration of the sympathetic fibres, than if the pre-ganglionic fibres have been divided, leaving the distal neuron intact,[60] but this sensitivity is not important in man (p. 169).

The maximum sensitivity to adrenalin occurs about the tenth post-operative day, and gradually decreases in degree until at the end of eighteen months it is practically non-existent. Now relapse following sympathectomy, except in a very few cases of relapse within a few days, rarely occurs until after the sixth month, when adrenalin sensitivity is markedly less than it is ten days after operation, and whereas the relapse tends to progress in severity, the adrenalin sensitivity decreases with the passage of time. It does not therefore seem that post-sympathectomy adrenalin sensitivity is a factor of significance in explaining the clinical recurrence of Raynaud's phenomenon after sympathectomy.

2. **The condition of local vessels.**—One of the observations on which Lewis based his theory of local sensitivity to cold was the fact that sympathectomy did not always prevent vasospasm, and even if it did there was a marked tendency to relapse. It is well known that in what have been called early cases of Raynaud's disease, but are now considered cases of primary Raynaud's phenomenon, the early results of sympathectomy are invariably good; but that if the operation is done for severe cases with trophic changes in the fingers the results, even in the early post-operative weeks, are often disappointing. In the latter condition there is narrowing or obstruction of the digital arteries and local cold alone is sufficient to cause spasm of such a degree as to result in complete stasis In any condition in which the digital vessels are diseased, such as scleroderma or thromboangiitis obliterans, the results of sympathectomy vary with the degree of arterial obstruction Where atherosclerosis with obstruction of the larger vessels higher in the limb is the origin of the Raynaud's phenomenon, sympathectomy gives good results as the total blood-flow to the hand is increased significantly by the dilatation of the collateral vessels around the obstructed segment of larger artery.[17]

It does not seem that there is any peculiar change in the digital vessels which renders them sensitive to cold, but rather that stasis of blood-flow is due to the normal reaction to cold on vessels which are narrowed or obstructed. Therefore it is the extent of the local disease which determines the severity of the vasospastic attacks, and it is those patients with severe disease who have early recurrence of symptoms after sympathectomy.

3. **Recurrence of sympathetic activity.**—Sympathetic nerve fibres seem to have a remarkable facility for regeneration.[61] Smithwick describes regeneration of a splanchnic nerve which appeared normal on a second exploration, and he would have doubted its removal except for the presence of a silver clip on the nerve which had been applied on the first occasion In every case of late relapse which we have tested we have found without exception that there is evidence of sympathetic activity, as shown by increase of skin temperature

of the little finger following ulnar nerve block. In hands which show no clinical relapse there is no evidence of sympathetic function. Barcroft *et al.*[47] reported recurrence of sympathetic activity six to nine months after sympathectomy in cases which they investigated, although symptoms were not always commensurate with the degree of activity present (p. 179). Felder *et al.*[46] who repeated the experiments of Simmons and Sheehan showed that the degree of relapse bore a very close relationship to the degree of recurrence of vasomotor activity. Most surgeons with experience of peripheral vascular surgery have re-operated on relapsed cases, generally by doing a root section *via* the posterior approach if the previous operation has been an anterior

discussed the problem of regeneration and has produced evidence that it occurs in man He dissected at autopsy the sympathetic trunk in the cervico-thoracic region in a woman who had a cervico-thoracic sympathectomy fifteen years previously, which had been followed for a year by complete freedom of symptoms, with later recurrence. He found the chain to be reconstituted, with a gangliform enlargement and numerous rami connecting it with the nerves of the brachial plexus.

In a careful and detailed follow-up of patients after sympathectomy, it was found that 60 per cent. were cured and 80 per cent. improved after the end of two years, but only 17 per cent. were cured and 37 per cent. improved after five years.[46] Published results do not, however, differentiate between cases of primary Raynaud's phenomenon and Raynaud's phenomenon secondary to obliterative disease, as in the latter group progress of the disease alone may lead to deterioration in the clinical condition, apart from any question of regeneration of sympathetic nerve fibres. However, generally speaking, the gradual deterioration of the clinical condition occurs *pari passu* with regenerating sympathetic fibres. From these figures it is seen that 17 per cent. of patients are permanently cured, and by "cured" is implied, "that attacks of vasospasm had not occurred after operation and could not be precipitated in the laboratory on exposure to cold"—and that in these cases there had been no laboratory evidence of regeneration

It must be noted, however, that
is never sufficiently marked to
detected in the laboratory, and ... enophthalmos and contracted pupil after
stellate ganglionectomy never recover

Alternate anatomical pathways for the sympathetic nerves destined for the limb provide another possible explanation of regeneration.

Intermediate ganglia have been demonstrated scattered outside the sympathetic chain, in the communicating sympathetic rami, or actually within the substance of the spinal nerves or nerve roots close to the attachment of the communicating rami.[63, 64] Owing to their position these ganglia escape removal in operations for sympathectomy, and although their function is probably minimal in the normal individual, they may become more important following excision of the main sympathetic pathways. It could be argued that an early relapse would occur in those cases where anatomical variations were functionally important. However, it has been mentioned above that in the early relapses, *i.e.* those occurring within days, there is no evidence of return of vasomotor control. It may be that it takes some considerable time for the intermediate or other "ectopic" ganglia to assume activity in the limb.

The fact remains, however, that in the late recurrences sympathetic activity can always be demonstrated, whether as a result of regeneration or of activation of "ectopic" ganglia. Possibly both factors are operative.

It takes a variable time, up to five years, for returning sympathetic activity to become complete, and often it may never do so. Thus after sympathectomy for primary Raynaud's phenomenon, the results will be excellent at first, and in about 20 per cent. they remain so. In the remainder with the return of sympathetic activity there is some return of symptoms, but the attacks only reach their pre-operation severity in about 30 per cent. If the operation is done for moderate degrees of distal vascular obliteration, the percentage of successes can be scaled down, as even slight return of sympathetic function in such cases may be sufficient to induce an attack of Raynaud's phenomenon, and in cases with severe degrees of vascular obstruction, the results may be bad as local cold alone in association with this degree of obstruction is sufficient to produce complete vascular stasis.

The incidence of Raynaud's phenomenon in the toes is difficult to estimate and its clinical importance in this site is not great. The feet are generally, in cold weather at least, adequately covered by socks or stockings and are shod with wind and weather-proof leather Woollen lined boots and an extra pair of socks are frequently worn in cold weather. In primary Raynaud's phenomenon the toes are affected in about 30 per cent. of cases. In arteriosclerosis the toes are affected more often than the hands and in these cases lumbar sympathectomy is permanently effective. As a result of sympathectomy the condition is cured in the toes, and we have never seen a recurrence. In fact in those cases, when there is no apparent benefit, we believe that the operation has not in fact removed the lumbar sympathetic chain, and on two occasions where we have repeated the operation, this was found to be the case. Removal at this time resulted in complete and permanent cure of the symptoms. Why there is not the same tendency to recurrence of vasospastic attacks in the feet compared with the hands we do not know. We have followed

cases for seven years and there has been no clinical evidence of recurrence of sympathetic activity although it has sometimes been demonstrated.[6] It appears to us that the difference must lie in the anatomical arrangements of the para- [illegible] in the number [illegible]

that in the toes the results of sympathectomy are good—permanent as regards clinical recurrence of symptoms

INDICATIONS FOR SYMPATHECTOMY

[illegible] of symptoms following [illegible] ry Raynaud's [illegible] are not often severe and trophic changes do not occur. Abolition of intermittent spasm is not necessary for the prevention of permanent intimal thickening, as the natural history of such cases does not indicate that there is this risk.

However, there are some cases of primary Raynaud's phenomenon where the symptoms are sufficient to interfere with the work of the patient, or seriously to interfere with his or her comfort, and in these sympathectomy must be considered, accepting the fact that after a time recurrence of sympathetic activity will result in some recurrence of symptoms in many patients.

In cases where there is such a degree of vascular obliteration that local cold alone is sufficient to produce a Raynaud's phenomenon, sympathectomy will be valueless, and such cases can be detected by the fact that cooling the hand in water at 15°C. with the body warm induces complete vasospasm. In the intermediate cases the operation is of value in abolishing one of the factors concerned in the production of the phenomenon. Therefore whilst in advanced scleroderma and " Raynaud's disease " the results of sympathectomy are disappointing they are more favourable in the early cases. As the rate of progress of these conditions is variable the operation should be advised in those cases which on indirect heating or other tests show ability of the vessels to dilate significantly but the patient should be warned that though improvement will occur, the condition of the hands and fingers may not return to normal We do not agree with waiting until severe trophic changes are present before advising sympathectomy, because by this time extensive disease of the digital vessels will preclude a good result. On the other hand, if the patient is first seen when digital artery obstruction is advanced, sympathectomy should still be considered, provided local cold alone does not induce an attack of vasospasm. Painful terminal ulcers are almost always healed.

In Raynaud's phenomenon associated with atherosclerosis, when the larger vessels, and rarely *if ever the digital* vessels, are diseased, the results of sympathectomy are good. Similarly in thromboangiitis obliterans, before the digital vessels are extensively diseased, sympathectomy leads to marked

relief or even apparent cure of the vasospastic attacks, and usually to healing of terminal ulcers.

Although the benefits of the operation may often be limited, sympathectomy is at the present time the most effective method available for treating Raynaud's phenomenon, and if the limitations of the procedure are recognised and explained to the patient it is of real value.

The method of operation and its technique are discussed later in Chapter XXIX.

RESULTS OF SYMPATHECTOMY

The results of sympathectomy for Raynaud's phenomenon depend on two major factors, one the recurrence of sympathetic activity, and the other the progress of any vascular obliterative disease which has caused the phenomenon. Thus if the operation is done for a primary Raynaud's phenomenon, the results will always be good initially, and although there may be some recurrence of vasospastic attacks after a year or two, these rarely progress to their pre-operative severity.

If the operation is done in the presence of a severe degree of digital artery obstruction, then the results will depend on whether local cold alone is sufficient to cause complete vasospastic attacks, and if this is so, the operation will be a failure and early relapse will occur. If, however, there is a minor degree of digital vessel disease, then there will be improvement after sympathectomy, but there will be deterioration if the disease progresses, quite apart from deterioration due to regeneration of sympathetic nerves. At present we do not know which case of arterial disease will remain stationary, which will progress gradually over years, and which will progress rapidly. Those cases of arterial narrowing or obstruction which are non-progressive, such as those resulting from injury and cold, provided they are not so extensive as to lead to occlusion from local cold alone will behave in the same way as primary Raynaud's phenomenon following sympathectomy.

Thus, if all these factors are taken into consideration it is readily understood how published results have shown such enormous variation. One series gave a failure rate of 83 per cent.[49] whereas another gave a failure rate of under 6 per cent.[7] Other series give results between these two figures.[17, 46]

Generally speaking in established scleroderma and severe "Raynaud's disease" the results are poor, as the arterial disease is often extensive, but sometimes the life and function of a digit may be preserved. In thromboangiitis obliterans, operation is indicated, as the disease process is so variable. In primary Raynaud's phenomenon, results are good for a period and about one in five is permanently cured and most are relieved, and a similar result can be expected in Raynaud's phenomenon the result of injury.

If, therefore, only the most favourable cases are chosen for operation, the results will be much better, although this must not prevent the offer of the

measure of improvement that can be achieved from a comparatively simple operative procedure to patients with more severe symptoms, even if results are sometimes disappointing Sympathectomy is the most effective treatment known

P. M.

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CHAPTER XV

ARTERIAL TRAUMA

An artery may be damaged by a crushing injury, a severe blunt injury, dislocation or fracture,[1] by the passage of a missile or stabbing weapon through the artery or through a part of it, or by the "lateral concussive effect" of a high-velocity projectile which passes near the vessel without actually touching it. In civil practice open wounds of arteries are usually caused by fragments of plate glass or, in factories, by fragments of steel or by parts of moving machinery. Arteries may also be damaged at operation, the femoral artery, for example, during the operation of saphenous ligation. The injury may give rise to arterial spasm, or contusion, with or without thrombosis; partial or complete division may give rise to a false aneurysm (pulsating haematoma) and partial, or more rarely, complete division may give rise to arterio-venous fistula if the vein is simultaneously injured. Partial or complete division may be followed subsequently by secondary haemorrhage. These effects of arterial trauma will be considered in turn.

TRAUMATIC ARTERIAL SPASM

Two varieties of traumatic arterial spasm are described—a benign and a malignant.[2] The benign variety follows direct trauma from a "near miss," or from handling, or from "twanging" of the artery. The malignant type occurs in crush injury, the brutal application of a tourniquet,[3] or the local concussion of a small mine. There may be local bruising of the vessel wall, but this is rarely extensive. The artery most frequently affected by traumatic arterial spasm is the brachial, which suffers most often in its lower third after supracondylar fracture of the humerus. Traumatic spasm of this vessel seldom extends proximally above the upper level of the origin of brachioradialis, but it often extends distally into the forearm, and the spasm may persist for long enough for the forearm muscles to develop contractures. In the lower extremity the distal third of the femoral artery, the popliteal and the posterior tibial arteries suffer most commonly, often after fracture or run-over accidents.

Spasm may mimic exactly complete arterial division. It may produce the same immediate ischaemic effects, but these seldom proceed to gangrene. It may affect only a few inches of a main vessel, or the whole peripheral arterial tree of an extremity. The affected vessel is white and contracted to its limit. The spasm is usually transient, lasting not more than twenty-four hours, but it may persist even when adjacent tissues are dying or dead. Sometimes it is intermittent.

Intense spasm of an artery is the property of the muscle of its wall and it occurs independently of the artery's nervous connections. It can be induced

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and to insert a graft to prevent subsequent secondary haemorrhage or aneurysm formation.

COMPLETE DIVISION OF AN ARTERY

This is manifest in external arterial haemorrhage and, if the vessel is sufficiently important, the symptoms and signs of arterial interruption. Both ends of the artery, for a distance of an inch or so, contract into their sheaths in spasm, shortening in length and narrowing in diameter, so that spontaneous closure may occur.

The local haemorrhage should be controlled immediately by pressure, artery forceps or ligature; the use of a tourniquet is a sign of failure, and more limbs are lost than lives saved from tourniquet application.

At *operation*, repair by axial anastomosis is rarely possible. Towards the end of World War II the possibility of immediate vein grafting began to be considered,[5] and vein graft would now be generally regarded as the most suitable method of repair. Vein graft is generally employed for repair of a gap too long for anastomosis. A segment of saphenous vein is inserted, its distal end being joined by suture to the proximal end of the artery, its proximal end to the distal end of the artery, so that its valves lie open to the arterial stream.[6] Alternatively, the insertion of a polyethylene, lucine or cloth tube has been advised,[7] though this is generally inferior to vein graft.

If grafting is for any reason undesirable, if, for instance, the wound is badly contaminated, both arterial *ends are ligated*. It seems immaterial whether the companion vein be simultaneously ligated or not. The arterial ligature is placed as close to the arterial lesion as possible, though Holman[8] advises that it be placed immediately below the next highest collateral to avoid the buffer effect of a blind end—he found the pressure in the collateral 10 mm. of mercury higher if the ligature was close up to its origin. At operation, injury to collaterals, especially muscle branches, is avoided. The artery is not ligated in continuity—every ligated vessel, whatever the cause of ligation, is divided across; pulsation against a fixed point leads to necrosis whereas pulsation against a mobile blind end does not. Triple ligation at a bifurcation is avoided—blood should be able to sweep smoothly across a bifurcation.[9]

When the patient is returned to bed he will often require a continuation of anti-shock measures, and available methods of encouraging collateral circulation are instituted as well as those for the care of an ischaemic limb. Blood transfusion, oxygen administration by B.L.B. mask, [illegible]
morphia, local cooling of the [illegible]
Sympathectomy is of d[illegible]

[illegible] limb, may save the life [illegible] and even four litres of blood may be given before the limb assumes the appearance of viability.[10] Plaster is not applied to encircle

in the isolated artery of the umbilical cord and it is frequently seen at operation as a result of nipping or pinking an artery with forceps. The effect of the spasm on the extremity is exaggerated (*a*) if important collaterals have their mouths of origin in the contracted segment; (*b*) if important collaterals have been damaged by the missile which has produced the spasm; (*c*) if the collaterals are also spastic, and (*d*) if the patient is at the time in the vaso-spastic stage of haemorrhagic shock.

Since spasm cannot be differentiated clinically from complete interruption or from thrombosis the affected vessel is explored. When it is found to be spastic it is gently washed clean with warm saline. Kinmonth[4] has shown that a sponge soaked in 2·5 per cent. papaverine relaxes spasm that has been experimentally induced, but that neither this relaxant or any other available drug given arterially seems to have any effect. This should be tried. If it is not effective, and it is not always so in traumatic spasm in man, firm rolling of the affected vessel between the fingers may sometimes result in complete relaxation of the vessel. *Stripping of the artery is not done*, and only if the vessel is severely contused is the involved segment excised, continuity being restored by an autogenous vein graft. In the absence of bruising it is wise to *rely on the natural tendency of the vessel to recover. Only if collaterals have* been extensively damaged, and the limb is dependent on the spastic vessel, is an attempt made to overcome the spasm by forcible proximal injection of *saline. After the patient's return to bed all available methods are employed* for the encouragement of collateral circulation.

ARTERIAL CONTUSION

Contusion depends for its effects upon the presence or absence of thrombosis in the contused segment. If no thrombosis is present the artery, or a patch on its wall, is discoloured, but pulsation is still present in it. The only danger of such a contusion is subsequent aneurysmal dilatation, or secondary *thrombus formation, with arterial occlusion later, or distal embolism.*

When the contusion has been productive of thrombosis at the site of *the injury the artery is swollen, discoloured, solid* and non-pulsatile or only feebly pulsatile. The circulation is interfered with, and secondary haemorrhage may follow. Traumatic arterial contusion with thrombosis can be *differentiated neither from traumatic spasm nor from* complete interruption. The affected vessel is therefore explored. If it is severely contused or thrombosed, the affected segment is excised with a good margin of healthy vessel *on either side of the injury, and a graft is inserted.* If the vessel is found to be merely contused, and not the seat of thrombosis, it is difficult to decide what course to adopt. It was formerly considered advisable to fortify the *damaged segment* by a barrier of fascia or muscle, but this often leads to later aneurysm formation. If there is doubt about the degree of damage done to the wall of the artery, is is probably best to excise the affected segment

in the proximal segment of the artery and this is best treated by the local application of a sponge soaked in 2·5 per cent. papaverine. The vessel itself is carefully cleaned and the decision is made to graft if it is injured. Longitudinal or transverse suture leads to thrombosis or secondary haemorrhage. It is better to divide the artery completely, to excise the traumatised wall and to restore continuity by end-to-end anastomosis. For this, the arterial segments are well mobilised, even with the division of some adjacent collateral. The open ends are brought together in a triangulated way by three everting stitches and the anastomosis is completed by a continuous everting stitch. If too great a length of artery has been damaged to permit anastomosis without tension, a vein graft is best inserted. The artery, thus repaired by anastomosis or by graft, is covered by the immediately overlying soft tissues, but apart from this the muscle and skin are left open for five days. If the injury is in the lower limb, that limb is immobilised in a posterior splint; if the upper limb has suffered, it is bound to the chest. Repeated transfusion is essential to limb circulation after operation, and antibiotics are given for a day or two. If the colour of the limb is poor, sympathetic block may be done two or three times daily, and occasionally it may be considered desirable to establish continuous caudal block by an indwelling needle or plastic tube for twenty-four to forty-eight hours. Secondary operation for haemorrhage is sometimes necessary. If there is a fracture at or below the arterial injury, amputation should be considered, especially in the case of the femoral artery; fracture of the femur associated with an injury of the femoral artery and wide [illegible]

[illegible] traumatic aneurysm a week or two, or even more, after wounding. The local reaction of the tissues to injury at this stage, and the effects of local haemorrhage, make the operation of anastomosis or grafting difficult. Exploration is therefore best postponed for a few weeks more, when a traumatic aneurysm has formed. During the weeks of waiting the limb is closely watched, for urgent intervention becomes necessary if suppuration is established, if external haemorrhage occurs or if the aneurysm grows so rapidly that collaterals are threatened.

SECONDARY HAEMORRHAGE

Secondary haemorrhage is usually due to a partial division of an artery, in combination with sepsis. Sepsis alone rarely causes secondary haemorrhage by digestion of the wall of a ligated vessel, together with its ligature. Sometimes the lateral wound in the vessel is produced by a mobile bone fragment, the vessel wall having been already weakened by sepsis. It is always wise to assume that secondary haemorrhage is due to partial division of an artery and to seek the actual point of injury, opening the septic wound below a sphygmomanometer tourniquet. Blind proximal ligation is seldom beneficial, for, when it is performed, collateral channels have already opened, a substan-

completely the wounded extremity, whatever fractures are present in it, if there are any doubts of its vitality. Massage is not permitted, though frequent passive movements of the smaller joints are encouraged to avoid "frozen" hands or feet. A close watch is kept for secondary haemorrhage, and for subfascial haematomas in the affected limb. The latter may require decompression by fasciotomy, and this should be performed, when necessary, at some distance from the previous wound so that the musculo-fascial barrier around the damaged vessel may retain its integrity.

PARTIAL DIVISION OF AN ARTERY

When an artery is incompletely divided, the attempted retraction of its ends increases the size of the lateral opening in its wall. The artery then continues to bleed or bleeds intermittently, either externally, as a variety of secondary haemorrhage if the soft tissue wound is large, or with the formation of a pulsating haematoma (traumatic aneurysm) if the soft tissue wound is small. If the vein is simultaneously injured, an arterio-venous aneurysm or aneurysmal varix may result. Sometimes the lateral wound in an artery is closed by clot, this later expanding as the sac of a traumatic aneurysm. Rarely the ends of a completely divided vessel are held together and prevented from retracting by the tension of locally attached branches, and the complete division may behave as a partial one—this situation has occurred in the root of the neck, in the groin and in the calf, but is not restricted to these situations

After partial division of a vessel there may be intermittent bleeding for a time, or there may be secondary haemorrhage after a few days, or there may be no symptoms of severe vascular injury at all until an enlarging aneurysm begins to threaten the distal circulation.

The treatment of open arterial injuries has been revolutionised by the experiences and researches of U.S Army surgeons in the Korea campaign. Before that campaign it was customary to encourage if possible the formation of a musculo-fascial barrier over the arterial defect to permit a traumatic aneurysm to form, so that collaterals might develop while the circulation continued through the damaged vessel. It now seems clear that if a patient in whom an arterial injury is suspected is seen at an early stage after wounding, the artery should be explored.[10, 11] The damaged portion of the vessel is excised and replaced by an autogenous vein graft or by a homograft obtained under aseptic conditions from patients with fatal wounds of the head or chest [12]

Transfusion and retransfusion are performed until circulation is stabilised The original tourniquet is replaced by a pressure dressing and a bandage, and the limb is X-rayed for foreign body or fracture. Débridement is then performed under general anaesthesia. The tourniquet is re-applied, or the vessel is exposed above the wound and a temporary ligature is applied proximally. Then the injury itself is exposed, and a serrated bulldog or Potts clamp is applied above and below the site of injury. Often there is obvious spasm

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is desirable. On the other hand, if the aneurysm is related to a vessel with a poor reputation for the development of collaterals (popliteal or internal carotid), or if there has been extensive soft tissue damage at the time of the original wound, or if sepsis is established, or if the patient is elderly, operation may be delayed for four to six months.

At operation, the vessel is controlled at a level above and well clear of the lesion by a sphygmomanometer cuff or by formal exposure and tape control. The classical endoaneurysmorrhaphy of Matas has many advantages. It avoids injuries to collaterals and to structures adherent to the wall of the sac, and it allows complete obliteration or sometimes even restoration of an arterial channel.[16] The sac is opened and the feeding and draining vessels are ligated within it, or joined by a vein graft if there has been threat to the limb. The sac can then be obliterated by suture together of its walls. The alternative to this operation is an external dissection, which may be employed if the anatomy of the part has not been too obscured by the processes of inflammation and repair. If external dissection is employed, Learmonth advises that the feeding artery be ligated close to the sac rather than below the next higher important collateral, as Holman[8] recommends, for Holman's ligation may exclude valuable muscular branches.

TRAUMATIC ARTERIO-VENOUS ANEURYSM[5, 9, 10, 11, 17, 24]

Usually an arterio-venous aneurysm forms by simultaneous partial injury of artery and vein, both vessels opening into a haematoma cavity, so that an aneurysmal sac communicates with both artery and vein (arterio-venous aneurysm). Less commonly the injury is followed by an immediate redirection, complete or partial, of the arterial flow into the lumen of the vein (aneurysmal varix). Sometimes the artery is doubly injured, and in addition to the arterio-venous aneurysm or aneurysmal varix there may be a purely arterial aneurysm related to the side of the artery opposite the vein. Rarely the proximal end of an artery, divided completely across, seems to heal in direct continuity with the distal end of a simultaneously divided vein. Usually there is an open wound, though rarely a fistula may follow a closed injury.[25] Arterio-venous aneurysms have sometimes been established by the transfixion and ligation of vessels at operation or by orthopaedic transfixion apparatus.[26] Exceptionally, an arterio-venous communication may be established by the fracture of a long bone. A curious and very rare type of arterio-venous fistula is that which may occur after such operations as nephrectomy or splenectomy, the artery establishing a direct end-to-end union with its companion vein after ligation of the vascular pedicle of the removed organ.

In general, the formation of the arterio-venous fistula resembles that of the pulsating haematoma, except that swelling is less pronounced, for the vein acts as a safety valve, the murmur, louder and audible earlier, proceed- to a machinery "grind," and a thrill [illegible]

tial circulation is passing through the injured vessel, and only local ligature will prevent recurrence of the haemorrhage. Local ligature for secondary haemorrhage of a vessel in leg or forearm is usually a successful operation. Ligation of the femoral artery for secondary haemorrhage after a shell wound with compound fracture of the thigh is so inevitably followed by gangrene that it is well to proceed to amputation straight away. In the Second World War lives would have been saved if the standard treatment of secondary haemorrhage from the femoral artery, in cases of compound fracture of the femur, had been amputation.

TRAUMATIC ANEURYSM. PULSATING HAEMATOMA

This is an affect of partial division of an artery. Initially the blood poured out from the lateral opening clots, but gradually the arterial pulsation, beating through the lateral opening, wears out an increasing cavity within the haematoma.[13] There is often a history of considerable primary haemorrhage from a small wound, and of a remarkable and persisting degree of local swelling disproportionate to the extent of the wound which is due more to oedema[14] than to haematoma—an oedema which assists localisation but impedes surgery. *The distal pulse usually persists, though diminished in volume and inconstant in its presence.* A persistent tachycardia is suggestive. A short systolic murmur develops in a few hours or a day or two, and should always be looked for when a wound track seems to pass near the line of an artery. At first it is merely a systolic whiff, best heard near entry or exit wound or where the artery is most superficial, but not propagated. In a few cases, particularly those of partial femoral injury, a faint cardiac systolic murmur is also audible. The systolic pressure in the distal vessels of the affected limb is lower than on the contralateral side. A good distal pressure and, better still, a wide distal oscillometer excursion, are the best evidence of improving collateral circulation.

The risk of a traumatic aneurysm developing can now be substantially lessened by the early dissection and exploration of arterial injuries, but if the original injury is overlooked, a traumatic aneurysm develops. If the arterial lesion is not suspected for a week or two after the original injury, *then the patient is managed conservatively for a total period of four to six* weeks after the wound has been sustained, in order that collaterals may develop to the full and the locality of the aneurysm be free of oedema. Operation becomes imperative only if there is a sudden increase in the size of the aneurysm, or if *interference with collateral circulation and nutrition* demand earlier intervention. The anatomical site of the injury is important too. In the neck, the axilla and the femoral triangle, where the tissues are lax, instead of the pulse beating out a sac in laminated clot, the extravasated blood may remain fluid, the hole in the artery being blocked by a small clot, which dislodges suddenly with rapid growth of the aneurysm after a few days, and compression of veins and collaterals;[15] in this situation, earlier operation

fistula, or by applying a temporary ligature there. When the sign is positive, the artery distal to the fistula pulsates, even though the main trunk is closed at the level of the fistula. The sign is important, because if it can be elicited ligation is likely to be relatively safe; if it cannot be elicited ligation is dangerous.

An arterio-venous fistula established in a growing limb, from whatever cause, may lead to skeletal and soft tissue gigantism.

Treatment

In World War II, arterio-venous fistulae were managed conservatively for about six weeks after their initial development. As a result of American experiences in Korea, it must now be regarded as desirable to explore any traumatic arterio-venous fistula within eight hours of wounding if possible. As in the case of other arterial injuries, the limb is X-rayed immediately and the patient is prepared for operation by liberal transfusion. Débridement of the wound is carried out and the fistula is widely exposed. Controlling tapes or Potts clamps are applied to the artery proximal and distal to the level of the fistula, and the vein is also doubly controlled. The vein is then separated from the artery and doubly ligated. It is not usually practicable to close the arterial vent through an opening in the vein which is subsequently ligated. Arterial ligation alone is inadmissible; if it is performed proximal to the fistula, the limb bleeds into its vein. The procedure of choice is reconstitution of the artery by anastomosis, vein grafting or artery grafting. This can best be undertaken early before pathological changes have occurred in the artery, altering its size and rendering its wall unsuitable for stitching.

Seeley and his co-workers[23] have recorded an experience of 101 aneurysms treated in Korea. A reconstitution was achieved in more than half of these, either by anastomosis, vein graft or artery graft. No anticoagulants were employed. Ninety of the patients were subjected to operation and sixty-four were found to have a major vessel lesion. Only 2·8 per cent. of the patients submitted to reconstruction showed signs of arterial insufficiency in the limb subsequently; this compares more than favourably with the 25 per cent. of insufficiency after ligation and 50 per cent. of insufficiency which occurs in lower limbs treated by ligation for main artery injuries. Chronic venous insufficiency occurred in two cases after reconstruction of the common femoral artery with sacrifice of its companion vein.

If the arterial injury has been at first overlooked, and the limb when the fistula is detected is the seat of inflammatory changes, it is desirable usually to manage the fistula conservatively for a period of a few weeks, until, say, six weeks after the causative wound has been sustained. If there has been extensive damage of soft tissues, or if the patient is elderly, operation may well be postponed for three or four months. Even after this period it may be possible to effect an arterial reconstitution.

pulsatile mass which, as it enlarges, erodes any bone which it encounters, and involves more and more of the vascular tree. The veins are particularly dilated and their walls thicken in "arterialisation." This need not necessarily follow, however, and the only physical sign may be the murmur. A machinery bruit is always present, loudest directly over the fistula and propagated down the artery.

Certain cardiac effects sometimes follow the establishment of an arterio-venous fistula. In general, the effect on the heart varies in degree proportionately with the size of the arterio-venous communication and its proximity to the heart, but this rule is not invariable; sometimes a peripheral fistula of relatively small size may produce a gross cardiac effect, while a relatively large fistula, quite close to the heart, may for long be unattended by cardiac effects. The first evidence of cardiac complications is a radiologically visible enlargement of the heart. The causes of this enlargement are disputed. The short-circuiting of large quantities of arterial blood to the venous side increases the rate of blood returned to the heart, and consequently the cardiac output, which may rise as much as 100 per cent., leading both to dilatation and hypertrophy. The increased circulation rate through the heart and rise in cardiac output are accompanied often by an increase in the blood volume. A clean wound and lack of scarring at the site of the fistula is almost as important as the size and position of the fistula in respect of the production of cardiac effects, for lack of scarring at the wound site and below it in the limb allows vaso-dilatation gradually to increase to the limit, and the amount of blood short-circuited and returned to the heart to increase progressively also. In some cases the heart dilates more than it hypertrophies perhaps because with the fall in peripheral resistance the diastolic pressure and consequently the mean aortic pressure are reduced with a lessening of coronary flow and impairment of nutrition of the heart muscle, interfering with hypertrophy.[17] The artery proximal to the fistula is affected also. It dilates and may become the seat of an arteriosclerosis which remains irreversible even if the fistula is closed. On occasion, the proximal artery has dilated to an extreme degree and has ruptured. A high proportion of experimental animals in whom large arterio-venous fistulas are produced develop endarteritis of the artery in the neighbourhood of the fistula.[27]

A dramatic physical sign of arterio-venous aneurysm is the bradycardiac reaction of Branham and Nicoladoni[29] If the fistulous artery is proximally compressed, the low peripheral resistance rises, for the leak into the venous sump is closed, the systolic pressure jumps up, and the pulse-rate slows. Like the cardiac effects, the Branham reaction is more likely to be obtained in the case of a proximal than of a distal fistula, but there is no close correlation between site and size of the fistula on the one hand and intensity of Branham's phenomenon on the other. Another interesting and important sign in arterio-venous fistula is the Henle-Coenen sign. This sign, which is always a late one, is elicited by compressing the fistula and the artery at the site of the

compartment of the leg may undergo ischaemia, often with a concomitant anterior tibial nerve palsy. It seems due to a rise of tension within the fascial compartment which is closed except at its lower end, though actual arterial injury or thrombosis has been blamed. Perhaps "shin-splint" of athletes early in their training is a minor form of the condition. Most patients are in their twenties and nearly all fall into the age group eighteen to forty. The muscles of the anterior compartment suffer, the extensor hallucis most and the extensor digitorum longus least. The extensor digitorum brevis, though not a muscle of the anterior compartment, quite commonly suffers too, a circumstance which makes it difficult to understand how the condition can be related to a high pressure within the anterior compartment. When the patients are convalescent, the main arterial trunk can be shown by arteriography to be open

There is usually a slight degree of foot drop, but such change as there is in the muscles is permanent and irrecoverable. The nerve lesion usually recovers in three months though in one case it seemed to be permanent and continued at all events for nearly five years Cessation of exercise and rest in bed for a day or two during the acute stage are essential. The condition seems to be pathologically analogous to Volkmann's ischaemic contracture, and perhaps it is a kind of traumatic arterial spasm

ENVIRONMENTAL EFFECTS ON THE CIRCULATION

FROSTBITE, HIGH ALTITUDE FOOT, IMMERSION FOOT AND TRENCH FOOT

1. FROSTBITE

Response to freezing.[1, 2]—When a limb is subjected to freezing the first signs appear at 15°C The extremities redden because of a relative oxygen surplus; the oxygen consumption is reduced more than the flow. At 10°C. the skin is definitely red and hypoaesthetic, and movements are clumsy. Below 10°C the skin is bright pink and painful The vessels are not completely contracted yet, but at still lower temperatures they undergo waves of contraction and dilatation, and finally close to the limit in the "white reaction" of Stray;[3] this is followed at minus 2·5°C. by the freezing of the tissues and the formation of ice crystals The part is anaesthetic, stiff, cold and white, with sometimes scattered areas of cyanosis. Even at this stage recovery may follow, and in some cases the tissues need not be greatly damaged because of the phenomenon of "super-cooling," or the capacity of tissue to be cooled beyond its freezing point without solidifying. The real level at which freezing occurs seems to be between minus 4°C. and minus 10°C. and freezing may not occur until a temperature of minus 20°C. is reached[4] The arteries and arterioles of the frozen part are intensely con-

In very late cases, when the fistula has been present for years, surgical management is exceedingly difficult. Whether or not operative intervention is advised then depends on the effect that the fistula has had on the nutrition of the part and the presence or absence of cardiac complications. If the heart is enlarged, operation should usually be undertaken. When operation is performed at this time, the artery is frequently found to be the seat of quite advanced degenerative disease. Anastomosis and ligature may both be prohibited by the state of the arterial wall. If it is thought that the artery will carry sutures, the fistula segment of the artery may be resected and the artery reconstituted, as in early cases, by anastomosis or graft. Disparity in size of the arterial ends is not in itself a bar to successful reconstitution. A plastic procedure may be undertaken by some form of Z-plasty, or by a longitudinal incision in the smaller vessel. When anastomosis is undertaken in these circumstances, interrupted mattress sutures are preferable to a continuous suture, and they should be placed one millimetre apart, each taking a bite of half to one millimetre.

If it is thought that the artery is not capable of holding sutures, there may be no choice but that of quadruple ligation, the artery being closed above and below the fistula, the intervening segment excised and the vein sacrificed. Sometimes even ligation of the artery is hazardous, and it may be thought best to close the proximal end of the artery, which is more diseased usually, by the insertion of sutures in it, after excision of the fistulous segment Quadruple ligation should not however be undertaken if the Henle-Coenen sign is absent, unless the condition of the patient absolutely demands it, and the state of the arterial wall absolutely forbids reconstitution.

A patient who has suffered for long from arterio-venous fistula may be seen first in an extreme state of cardiac failure. Usually then all considerations must give place to the closure of the fistula, and quadruple ligation is frequently the only choice. In exceptional circumstances, if the patient is in great distress, ligation of the vein proximal to the fistula may improve the condition of the patient sufficiently to allow a more radical procedure a little later.

Sometimes when a patient has a long-standing arterio-venous fistula, and particularly a fistula in the neck, face or scalp, the grossly dilated, tortuous and pulsating veins of the region may make operative intervention extremely hazardous, for in this anatomical situation bleeding cannot always be easily controlled by the occlusion of a single trunk. If such a patient shows no sign of cardiac decompensation he is best left untreated.

THE ANTERIOR TIBIAL SYNDROME[30-33]

It is convenient to include this syndrome here though it is doubtful whether it is indeed traumatic or whether, even if it is traumatic, it should not be regarded as a form of peripheral thrombosis.

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In very late cases, when the fistula has been present for years, surgical management is exceedingly difficult. Whether or not operative intervention is advised then depends on the effect that the fistula has had on the nutrition of the part and the presence or absence of cardiac complications. If the heart is enlarged, operation should usually be undertaken. When operation is performed at this time, the artery is frequently found to be the seat of quite advanced degenerative disease. Anastomosis and ligature may both be prohibited by the state of the arterial wall. If it is thought that the artery will carry sutures, the fistula segment of the artery may be resected and the artery reconstituted, as in early cases, by anastomosis or graft. Disparity in size of the arterial ends is not in itself a bar to successful reconstitution. A plastic procedure may be undertaken by some form of Z-plasty, or by a longitudinal incision in the smaller vessel. When anastomosis is undertaken in these circumstances, interrupted mattress sutures are preferable to a continuous suture, and they should be placed one millimetre apart, each taking a bite of half to one millimetre.

If it is thought that the artery is not capable of holding sutures, there may be no choice but that of quadruple ligation, the artery being closed above and below the fistula, the intervening segment excised and the vein sacrificed Sometimes even ligation of the artery is hazardous, and it may be thought best to close the proximal end of the artery, which is more diseased usually, by the insertion of sutures in it, after excision of the fistulous segment. Quadruple ligation should not however be undertaken if the Henle-Coenen sign is absent, unless the condition of the patient absolutely demands it, and the state of the arterial wall absolutely forbids reconstitution.

A patient who has suffered for long from arterio-venous fistula may be seen first in an extreme state of cardiac failure. Usually then all considerations must give place to the closure of the fistula, and quadruple ligation is frequently the only choice. In exceptional circumstances, if the patient is in great distress, ligation of the vein proximal to the fistula may improve the condition of the patient sufficiently to allow a more radical procedure a little later.

Sometimes when a patient has a long-standing arterio-venous fistula, and particularly a fistula in the neck, face or scalp, the grossly dilated, tortuous and pulsating veins of the region may make operative intervention extremely hazardous, for in this anatomical situation bleeding cannot always be easily controlled by the occlusion of a single trunk If such a patient shows no sign of cardiac decompensation he is best left untreated.

THE ANTERIOR TIBIAL SYNDROME [20-33]

It is convenient to include this syndrome here though it is doubtful whether it is indeed traumatic or whether, even if it is traumatic, it should not be regarded as a form of peripheral thrombosis.

After a period of exercise, or a sudden movement, or a leg transfusion which has been followed by extravasation, the extensor muscles in the anterior

resultant "hyaline masses" are responsible for the final and irreversible arrest of the local circulation, and for any subsequent tissue loss.

TREATMENT.—Thawing should be as slow as possible. The patient is nursed supine at an open window, with the frozen extremity or extremities elevated on a pillow and exposed to a cool draught. The remainder of the body is kept warm, and a normal extremity is heated in an air bath to induce gradual reflex vasodilatation in the frozen part. (It should be said here that Shumacker's Korean experience and some recent laboratory work suggest that more rapid thawing than this may be beneficial, but it seems likely that a strict thawing technique is an absolute requisite if speed is to be used, and a thoroughly safe management is not yet available in full detail.) Sulphanilamide powder is applied to blisters or ulcers. Full heparinisation may be begun as soon as the patient is seen, to limit the development or progress of thrombosis in the arterioles of the frozen extremity.[13] Massage is not permitted. Sympathetic interruption appears to confer no benefit and may be harmful. Areas of necrosis are kept sterile and removed by local excision when a line of demarcation has formed

Lange and Boyd[11] have devised a test for estimating the amount of tissue loss to be expected, and it seems reliable if performed within fourteen hours of exposure. They inject intravenously 10 ml. of a mixture 5 per cent. fluorescein and 5 per cent sodium bicarbonate, and inspect in a darkened room by ultraviolet light The entire skin surface shines green except where the skin is cut off from the circulation

Later, in convalescence, wax baths and exercises are arranged. The local circulation after recovery from frostbite is often extremely labile, and the part may show an exaggerated susceptibility to cold and heat It must be protected against extremes of temperature, and the patient is excused further service in a cold climate A frostbitten part is susceptible to frostbite, perhaps because of partial closure of its capillary bed by organised hyaline [illegible]
Causalgia sometimes [illegible]
fully treated [illegible]

2. HIGH ALTITUDE FROSTBITE

This does not differ greatly from simple frostbite, but occurs at substantially higher temperatures since the ischaemia produced by vascular spasm is exaggerated sometimes by the general anoxia of a low oxygen atmospheric tension and since wind exaggerates the effect of cold at any given environmental temperature.

3. IMMERSION FOOT. TRENCH FOOT. SHELTER FOOT. BRIDGE FOOT

These differ in several respects from frostbite. The term "trench foot" was invented in the early part of the First World War for the condition in

stricted, and the capillaries are empty, but cell metabolism has been suspended, and even long periods of oxygen-lack are well sustained.

Response to recovery from freezing.—Lewis believed that the tissue damage of frostbite was due to stabbing of the cells by ice crystal, yet ethyl-chloride freezing, which is productive of crystals, does not lead to necrosis It has always been generally thought that the effects of exposure to cold were more often due to recovery from freezing than to freezing itself, that the effects of low temperature in fact arise not from direct damage to tissue but from vascular reactions during cooling and warming.[5] This widely held belief may perhaps have to be revised in the light of Shumacker's experiments[6] on rapid thawing, and his observation that in Korea rapid thawing gave better results than a slow return to normal temperature.

When a patient's extremities are returned to a normal temperature after a short exposure, there may be no reaction except pain. If the exposure has been rather longer the skin reddens, its temperature is elevated, and it becomes thick and oedematous with itching or burning or pain. There may be residual pigmentation (first degree frostbite) or, after long exposure, blistering (second degree frostbite). If the tissues themselves have been frozen to ice and then allowed to thaw at room temperature, the colour of the skin changes to dull or sometimes bright red, and within two minutes there is a well-marked oedema. Wheals and blisters develop in the skin and sometimes necrosis. The development of oedema is slower if recovery takes place in the open air—indeed, both warmth and light accelerate the effects of thawing and it is notorious that frostbite is commoner in the sunny days of the late Norwegian winter than in the dark mid-winter.

Pathology.—The underlying pathology of thawing has been studied and agreed by many pre-war and war-time authors.[7-11] In the frozen part the arteries and arterioles are constricted, the capillaries occupied by a viscid mass of corpuscles, the plasma having leaked out through the capillary walls With warming, the arterial and arteriolar spasm passes off and the capillaries fill with blood. If cellular metabolism is resumed at once, some oxygen is abstracted from the capillary blood and that blood gives a dull red appearance to the part; if cellular metabolism is not immediately resumed, the blood in the dilated capillaries retains its oxygen and endows the part with a bright red colour. Because of the viscid content of the capillaries the resumed circulation is sluggish and in places static, and more plasma leaks out into the tissue spaces to increase the oedema and blistering, and the capillary content becomes a solid mass of corpuscles. This phenomenon, "conglutination," is the basis of the circulatory arrest which follows frostbite; true arterial or venous thrombosis may not occur even when the tissues are frozen solid though it supervenes after necrosis or with the onset of infection[12] and Shumacker has deduced that it may be present even in earlier stages. The viscid and conglutinated corpuscles undergo a curious necrosis, and the

resultant "hyaline masses" are responsible for the final and irreversible arrest of the local circulation, and for any subsequent tissue loss.

TREATMENT.—Thawing should be as slow as possible. The patient is nursed supine at an open window, with the frozen extremity or extremities elevated on a pillow and exposed to a cool draught. The remainder of the body is kept warm, and a normal extremity is heated in an air bath to induce gradual reflex vasodilatation in the frozen part. (It should be said here that Shumacker's Korean experience and some recent laboratory work suggest that more rapid thawing than this may be beneficial, but it seems likely that a strict thawing technique is an absolute requisite if speed is to be used, and a thoroughly safe management is not yet available in full detail.) Sulphanilamide powder is applied to blisters or ulcers. Full heparinisation may be begun as soon as the patient is seen, to limit the development or progress of thrombosis in the arterioles of the frozen extremity.[13] Massage is not permitted. Sympathetic interruption appears to confer no benefit and may be harmful. Areas of necrosis are kept sterile and removed by local excision when a line of demarcation has formed

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3. IMMERSION FOOT. TRENCH FOOT. SHELTER FOOT. BRIDGE FOOT

These differ in several respects from frostbite. The term "trench foot" was invented in the early part of the First World War for the condition in

men wearing puttees for long periods in cold water-logged trenches—especially during the winter 1914-15. Immersion foot has long been familiar to mariners. Shannon, marooned in 1832 for seven days in the Arctic, lost thirty of his company of forty-nine from this cause. *Shackleton and his comrades met it* on their trip from Elephant Island to South Georgia. It occurred among the survivors from the Titanic. It was frequent in the last war among sailors transferred with brine-soaked clothing to boats and floats which were often waterlogged. The effects are due to prolonged exposure to a degree of cold insufficient to freeze the tissues. The tissues freeze at minus 2·5°C., sea-water at minus 1·9°C., so tissues bathed in unfrozen sea-water cannot themselves be frozen but their wetness increases the conduction of cold to them and the loss of heat from them, so that the phenomenon of "super-cooling," which is protective against frostbite (*see* p. 541) does not occur. The feet suffer almost invariably, and feet hanging dependent in bilge-water are particularly susceptible. *In two-thirds of cases the hands suffer too.*[14]

During exposure and after a period of some hours to fourteen days the limbs become numb and the feet clammy and the patient "walks on cotton-wool." Pain, tingling and itching are unusual, but sometimes there are cramps in the calves. After hours or days bare feet swell and shod feet feel constricted The skin turns red, then pale, then yellow, blue and black. Sometimes in freezing temperatures at sea they are a vivid red.

After rescue, the immersed extremity passes through three stages.[15]

(*a*) *The first or pre-hyperaemic stage lasts for a few* hours to several days. The limbs are cold, swollen, discoloured, numb, powerless, and feel "as though they weren't there." The peripheral arteries may be impalpable and *gangrene may develop during this stage.*

(*b*) The second or hyperaemic stage continues for six to ten weeks The extremity is swollen, red, hot to the touch and painful, and returning sensation is heralded and accompanied by paraesthetic phenomena. There is weakness or wasting of muscles whose points of nerve-entry lie within the cold zone, and the skin undergoes blistering, ulceration, and sometimes during this stage too gangrene develops. The usual temperature gradients are absent and the digits are as warm as the groins or axillae. The extremities redden with dependency, blanch with elevation. Shooting pains occur and sharp stabs, often several at a time, at irregular intervals but more frequent and severe during the night. They may occur spontaneously or be evoked by warmth, *dependency, exercise, cold, micturition, defaecation,* coughing or yawning. Anaesthesia retains a glove or stocking distribution even if its area shrinks, but plantar or palmar surfaces are rather more widely affected than dorsal. The upper *limit of anaesthesia is irregular and loss of pain* is often wider than loss of touch, loss of heat sensation wider than loss to cold. The hair may fall out and nails may be shed. The general health suffers too during this stage. There is a low fever and loss of weight, *tachycardia, respiratory* and alimentary disorders, and sometimes albuminuria.

(c) The third or post-hyperaemic stage does not always occur. If it does occur it may last for weeks or months in the same form as the late effects of frostbite, hyperaesthesia; smooth, shining, hairless skin; pigmentation; telangiectases; hypersensitivity to extremes of temperature, and wasted and pointed digits with stiff joints. As after frostbite, one exposure predisposes to a second attack, even in less severe conditions.

TREATMENT.[16]—When rescued the patient should be treated as though suffering from a burn or a scald His boots and clothes are cut away, and he is carried and not allow to walk

(a) During the pre-hyperaemic stage the patient is warmed while his extremities are protected from heat though not overcooled.[17] He is put to bed between warm blankets, lying supine with his knees flexed vertically on a pillow. The affected extremities are exposed to the draught from an open window or from an electric fan, and kept dry. A distant normal extremity may be warmed to promote reflex hyperaemia Massage is not permitted. Penicillin-sulphonamide powder is applied to blisters and abrasions. Interruption of sympathetic paths during this stage has been advised by some, but Lake[19] and Greene[19] found it valueless and sometimes harmful.

(b) In the hyperaemic stage the limb is still kept cool. An environmental temperature of 21°C is usually equable,[20] but still more active cooling will relieve burning pain; even ice-bags are safe enough, for they do not much reduce the temperature of the tissues. Pressure dressings must be applied to limit the transudation of plasma.[21]

(c) Even during the post-hyperaemic stage the patient is kept in bed until swelling has gone and walking is painless. Buerger's gravitational exercises (p 454) are of benefit, and an arch support is worn until the small muscles of the sole have recovered their tone[17] Smoking is prohibited so long as vasospasm persists. It is in this stage and for the relief of vasopasm that sympathectomy is most useful,[22] and it is in this stage that late amputation may be required for persistent nutritional defects Pain of a neuralgic or causalgic character may require crushing of peripheral nerves

Trench foot,[23] which was commoner in the First World War than in the last war, does not materially differ from immersion foot; indeed it was immersion foot of a kind Fluid mud freezes at a rather higher temperature than brine, so that the immersed feet of the soldier were rather less cold than those of the sailor, but this inconsiderable advantage was offset by the soldier's vertical stance, the tightness of his puttees and ankle boots, and his low protein diet Shelter foot too presented few peculiar characteristics. Most sufferers from it had occupied deck chairs, and the transverse wooden bar over which the knees were flexed superimposed a mechanical pressure-occlusion of the popliteal artery. The patients were old too, and cardio-vascular disease and a poor physical condition exaggerate the effects of all forms of exposure to cold An additional factor in shelter foot is perhaps the

concomitant occlusion of the popliteal vein, which may add an element of stasis.

INTERRUPTIONS IN ARTERIAL SUPPLY BY EXTERNAL PRESSURE

1. LIGATION

Ligation of a main systemic vessel in a young person in his teens or even *twenties may be fully compensated, except in the case of the aorta and perhaps* the internal carotid artery, by collateral circulation. The popliteal artery, the common femoral, and the axillary below the subscapular branch have also an evil reputation. I have known the radial pulse return within twenty-four hours of brachial ligation, a profunda pulse being by then readily palpable at the elbow. *Conversely, ligation of a vessel is likely to occasion severe* nutritional inadequacy amounting to gangrene only in the elderly, when generalised arteriosclerosis prevents the establishment of an adequate peripheral circulation. In the ligation treatment of aneurysm, signs of impaired vitality were common, and were anticipated and treated by the usual measures for *incipient gangrene. Even in young persons, however,* coincident circumstances may exaggerate the nutritional effects of ligation of a main vessel When the femoral artery, for instance, is ligated in the depths of a shell-wound the wound has usually disrupted many collateral vessels of greater or less importance, and the number of these divided may be so great that nutritional change follows ligation; even when a femoral artery is ligated after its clean division by a high-velocity bullet, though no skin devitalisation may result, there is nearly always some muscle ischaemia, particularly if there has been substantial blood loss at the time of injury; the effects of ichaemia are always greater in anaemic and anoxaemic subjects. Infection is important too. Ligation of the femoral artery, performed to stay secondary haemorrhage from an infected wound of the thigh, is almost inevitably followed by amputation; and ligation of the brachial artery, performed to control secondary *haemorrhage from a septic hand, is nearly always followed* by gangrene and loss of one or two fingers

If gangrene follows ligation it is usually safe to delay amputation until a line of demarcation forms, but if there is infection in any part of the affected extremity, amputation is performed at once, clear of sepsis

It has been shown by experiment that it makes little difference to the development of peripheral circulation whether the companion vein be ligated simultaneously with the artery or not, vein ligation certainly promises no improvement

2. GANGRENE FROM BANDAGES AND SPLINTS

Bandages, splints and plaster casts may produce vascular occlusion in two different ways.

(*a*) The edge of a splint or plaster cast may compress an area of skin and occlude its vessels. This compression effects a local cessation of *circulation*

without previous oedema, a form of "direct traumatic gangrene." A dry ... slough forms which separates by line of demarcation to form ... be produced from within, when the ...

Sometimes healing can ... by skin grafting One of us (P. M) has in his care a child aged seven ... gangrene of this type in the skin of the foot. There was some doubt whether the gangrene was a direct traumatic gangrene or the more serious indirect variety whose description follows in the next paragraph. Arteriogram however showed an almost normal arterial tree. The gangrenous skin was accordingly excised and grafted, and the feet were saved, though all the toes were lost, presumably because they were affected by an indirect gangrene while the skin of the foot was affected by direct pressure. Arteriography may be helpful in such a case when there is doubt whether the gangrene is direct or indirect.

(*b*) When, however, a plaster cast or bandage is too tightly applied the veins are first occluded. Oedema follows venous congestion and the tension rises within the plaster until the arteries too are compressed; gangrene of the encased limb follows unless the constriction is released. Pain is the only ... of this melancholy complication and must be seriously regarded ... blue they can still ... occurred, and sometimes the subungual vessels seem to empty ... id refill with release of pressure, so no reliance should be placed on these tests as evidence of vitality while the limb remains in plaster. Pain alone is sufficient evidence, and there is no mistaking the severity of this form of ischaemic pain. Since the limb is oedematous before its arteries are occluded, gangrene if it occurs is moist, yet if reasonable precautions are taken there is little risk of infection, and amputation may be performed close to the highest point of constriction.

3 BEDSORE DECUBITUS ULCER

The bedsore is a form of gangrene from pressure The whole thickness of the skin is compressed to the point of anaemia between bone and mattress[21] It is particularly liable to occur in the aged, who are often relatively immobile and poorly cushioned with fat, and in paralytic patients and if the serum proteins are low from malnutrition In the paraplegic the sore may result from the upward tension on the skin of an anterior bony prominence, the iliac spine or the head of the clavicle The skin over the sacrum suffers most commonly in supine patients, the skin over the ischial tuberosities in sitting patients A dry eschar usually forms and separates to leave a relatively clean ulcer whose floor is of bone with a few tendinous strips of muscle origin. Sometimes, particularly if the patient is in any case dropsical, the bedsore is preceded by gravitational oedema; a moist form of gangrene then occurs not devoid of the risk of infection

In prophylaxis, an aged or paralytic patient is afforded the bed exercises and skin toilet which are routine for all bedridden patients, but in a fuller measure. The position is changed to the prone or lateral for periods of several hours daily. Four hourly the skin of the back is washed, massaged with spirit, and dusted with powder. The slightest persistent colour change, which in its earliest phase is a dull coppery red, is reported, and the position is altered to relieve such an area of all pressure. A water bed is desirable if the supine position must be maintained. Malnutrition under negative protein balance should be corrected.

Once a bedsore is established it is best treated by excision.[25] All infection is eradicated by chemotherapy, the area is adequately drained, pressure is avoided, the patient is frequently moved to prevent new sores, the ulcer is widely excised, the resultant defect is closed by a whole thickness rotating flap from the flank,[26] and the raw area in the flank, if it cannot be closed by suture, is covered by split-skin grafts. If the patient's condition is too poor to permit excision and flap closure at one stage the ulcer can be excised at a first stage and temporary cover applied by split skin. Closure is facilitated and recurrence of pressure is avoided if underlying bony prominences, the ischial tuberosities for instance, can be excised.[27] Healing is often prevented by the involuntary muscle spasms of paraplegic patients and these may require abolition by a selective anterior rhizotomy, each anterior root being electrically tested in turn to observe cystometrically whether it is concerned in bladder innervation.[26, 28]

NUTRITIONAL LESIONS PRODUCED BY CHEMICALS

Carbolic acid or lysol, applied accidentally or in ignorance as a wet dressing, was formerly notorious for the production of digital gangrene. Its anaesthetic effect abolished the danger-signal of ischaemic pain and when after some hours the dressing was removed the digit would be found shrunken, pale, numb, wrinkled and dead. Treated conservatively, a clear line of demarcation would form with separation of the dry digit as a mummified eschar. Gangrene of this type was due to combination of effects. The phenol, penetrating the digital tissues, coagulated the blood within the capillaries and coagulated too the protein of the cells. Lysol gangrene may develop in a baby born into a pool of strong lysol

I have observed an identical appearance in a finger blocked by procaine-adrenaline anaesthesia for removal of a needle from the pulp The ring of anaesthesia had been produced at the level of the middle phalanx, and whether the vascular interruption was due to high tension of interstitial fluid or to direct damage to both digital vessels was not known, nor was the part, if any, played by adrenaline; perhaps the adrenaline content of the anaesthetic material was high. A peculiar feature of the gangrenous finger-tip was the persistence of pinprick for some days after the other modalities of sensation

had disappeared and after the epidermis was shrunken, wizened, brown and hard

NUTRITIONAL LESIONS DUE TO THE INTRA-ARTERIAL INJECTION OF DRUGS[29]

The accidental injection of thiopentone into an artery is liable to be followed by gangrene. Gangrene has also followed accidental arterial injection of iodine compounds for pyleography, cholecystography or arteriography, ethamolin intended for a varicose vein, quinine for malaria, arsphenamine for syphilis, bismuth, transpulmin and myanesin There is no record of gangrene after the intra-arterial injection of perabrodil or pyelosil. Hartmann's solution and plasma injected accidentally or intentionally into an artery have produced gangrene Pentothal has been the commonest offender, perhaps 1 in 55,000 pentothal injections being followed by distal tissue loss No gangrene has been reported from evipan It seems that deep venous thrombosis may sometimes have the same effect, and the disappearance of arterial pulse and development of gangrene are not necessarily evidence that the injection has been made into an artery (*see* Phlegmasia caerulea dolens).

In the gangrene due to intra-arterial injection of pentothal, temporary obliteration of the subclavian or axillary pulse by a strained shoulder posture may permit an ascent of the drug against the arterial stream and lead to persistence of the drug within the vessel in high concentration for a time. After an injection the pulse may disappear or it may remain and disappear after an hour, or hours or days, or it may disappear, reappear for a time, and disappear again If 2 ml. is injected there is severe pain like "boiling water" or "flame" There is intense transient vasoconstriction of the distal parts. Sometimes there is general collapse and carpopedal spasm with disappearance of the opposite pulse, perhaps an effect of idiosyncrasy There is initial pallor of the distal extremity, which remains ashen grey or proceeds to cyanosis. The condition seems to be due to thrombosis in the major vessel. If the injection is into the radial artery, sometimes there is ascent to the brachial and again the forearm may be lost. If the injection is into the ulnar artery, the commonest error, it is not likely to ascend to the brachial and gangrene is limited to the fingers In addition to gangrene there may be Volkmann's contracture or paralysis of the distal peripheral nerves Extensive oedema is common and is a reasonably good sign—fingers that develop oedema do not become gangrenous Limbs that recover may show the Raynaud phenomenon later just as they do after frostbite

In most patients who suffer this accident there is arterial abnormality; in 10 per cent. of subjects there is high bifurcation of the brachial artery, the ulnar artery passing superficial to the common flexor origin and presenting for the needle This is the commonest anatomical cause of accidental artery injection Thrombosis is an essential pathological feature of the lesion. The needle prick is not responsible—this accident does not occur after arterial

puncture. The cause of the thrombosis seems to be sensitivity of the intima to thiopentone, perhaps because of its high *p*H. The thrombosis extends proximally to the next highest collateral above the upper limit to which the injected material reaches. Myanesin produces an artery block by flocculating the blood and liberating multiple tiny emboli. Some cases seem to be due to thrombosis or spasm of peripheral small vessels, for the pulse may persist at the wrist.

The accident may be prevented by close inspection for arterial pulsation, by avoidance of the veins in the cubital fossa for use in intravenous work, by avoiding hyperextension of the elbow, by using always a good light, by ensuring that the venous tourniquet employed is not tight enough to occlude the artery and by pausing after the injection of a small initial quantity to see if there is pain.

When the accident is detected, heparin should be injected into the affected artery and anticoagulants should be continued over a few days. Brachial plexus block is advised by some to abolish spasm. The patient is kept warm and the affected limb is elevated and slightly cooled. If symptoms are immediately severe at the time of injection and if extreme pallor of the distal limb seems to promise gangrene, the artery may be explored for thrombectomy or grafting.

I. A.

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CHAPTER XVI

VASOSPASTIC RESPONSES TO ENVIRONMENTAL COLD

WHEN the extremities are exposed to acute reductions of environmental temperature frostbite develops, or, if the environment is wet as well as cold, immersion foot. In addition to frostbite and immersion foot, and to Raynaud's phenomenon which is also in a sense a reaction to cold, there are other forms of response or reaction of the peripheral circulation to repeated low-grade reductions in the environmental temperature of a susceptible subject, in which the skin and underlying tissues of the exposed parts develop changes in colour, in constitution and, if the exposure to cold is continued, in integrity. One of the commonest types of such a response or reaction is acrocyanosis, a distinct clinical entity in which exposure to cold is the only consistent causative factor. At the other end of the scale from simple cyanosis on exposure to cold is a condition which involves chiefly the legs of women and is characterised by the presence of nodules in and sometimes ulceration of the skin. An attempt has been made to divide the progressive stages of this latter disease into a number of distinct clinical entities, an attempt which has not added to the understanding of this response to low-grade cold. We believe that there is a single process involved in such conditions and that any attempt to divide it into a number of clinical entities is not only impracticable but also unnecessary.

In all reactions of this type tissue ischaemia of varying degrees is the responsible factor, being produced by an inherently exaggerated vascular susceptibility to cold. The modes of response of the skin and subcutaneous tissues are limited regardless of the insult applied and no doubt the individual threshold of the inborn susceptibility of the patient's vascular system to cold governs the severity of the tissue reaction which develops and so, to some degree, decides which of the following clinical entities will predominate In practice the conditions are often found in association with each other.

LIVEDO RETICULARIS

Livedo reticularis or cutis marmorata is a not uncommon condition characterised by a blotchy, reddish-blue discoloration of the skin of the extremities. In many respects it resembles acrocyanosis but in contrast the colour changes are never diffuse and also it is the legs and arms which are mostly affected rather than the hands and feet Seen almost equally in both sexes, the condition is closely allied to other vasospastic disorders in which excessive arteriolar vasoconstriction is the prime abnormality In this, as in

acrocyanosis, the mechanism is thought to be an arteriolar spasm associated with circulatory stagnation in the capillary bed and sub-papillary venous plexuses If the spasm is severe and widespread a deep, diffuse cyanosis results (acrocyanosis) whereas if it is less severe the colour changes are patchy and reticular. From these colour changes the condition gets its name.

The symptoms of livedo reticularis are usually mild and many people go through life completely unaware that their response to cold is abnormal. An occasional patient may complain of coldness, numbness and paraesthesia of the limbs, but in the majority of cases it is the colour changes *only* which draw attention to the disease. The bluish-red mottling is more pronounced in the cold weather, when it may extend to the thighs and more rarely to the trunk. It is frequently present in association with other members of this group of conditions, *i e.* acrocyanosis and chilblains, of which it is probably a variant (Fig 314). In severe cases the colour changes persist even when the patient is in a warm environment and in rare instances ulceration of the skin of the legs and gangrene of the toes has been reported even though the major arteries have been normal. It seems more probable that when such severe trophic manifestations develop the livedo reticularis is an associated phenomenon not itself responsible for such gross tissue damage. When ulceration and gangrene develop a careful search must be made for a more serious arterial disease We have never encountered trophic complications in a limb solely as the result of livedo reticularis

The pathological changes in the tissues are not at all specific and resemble closely those described in acrocyanosis and chilblains Intimal proliferation and, rarely, occlusion of arterioles and venules has been described but in most instances biopsy reveals nothing more than a variable degree of hypertrophy of the muscular coat of the arterioles. Livedo reticularis has been described in association with polyarteritis nodosa, syphilis, hypertension, hyperthyroidism and many other general diseases, but the influence of such conditions as etiological factors cannot be assessed The widespread incidence of livedo reticularis in the general population points to a purely coincidental association probably related in many individuals to lowered general health and resistance to cold

The importance of livedo reticularis rests almost solely on the fact that it is unsightly In the vast majority of cases complications never develop and the condition does not progress so that reassurance of the patient with advice to protect the extremities from cold and to avoid body chilling is all that is needed In the rare case in which complaints are severe, or if complications develop, and it can be shown that there is no more serious arterial disease, sympathectomy may be tried. This should ...

... of lasting benefit ... that the operation

ACROCYANOSIS

The terms acrocyanosis and acroasphyxia are applied to a bilaterally symmetrical blueness and coldness of the hands and, less commonly, the feet of susceptible individuals upon exposure to moderate cold, particularly when combined with body chilling. There is no sex difference and there is no intermittency of attacks so that the condition should seldom be mistaken for Raynaud's phenomenon, the only vasospastic disease with which it might be confused.

Actiology.—The only aetiological agent of any importance is cold Cold is probably the precipitating factor in individuals who for some reason, as yet unknown, have blood vessels in the skin of their extremities abnormally susceptible to the vasoconstricting effects of cold. As with many unexplained vascular phenomena in the limbs functional derangement of the sympathetic nervous system has been postulated as a cause of acrocyanosis However, the careful studies of Lewis and Landis[9] have been substantiated by others[14] and leave little doubt that the mechanism and site of the vascular fault is an increased tone in the arterioles of the skin. Since everyone does not become an acral cyanotic upon exposure to cold a local fault, an abnormal susceptibility or a hypersensitivity to cold of the responsible blood vessels as an individual aberration, must be assumed to explain the unusually high state of arteriolar tone which exists in acrocyanosis. That the venous tone is not substantially increased, in the major veins at least, can be demonstrated by elevating the cyanotic limb which blanches slightly; this effect of elevation indicates that there is no obstruction to the venous outflow from the hands That the vascular fault is local rather than central in origin can be demonstrated by noting the immediate reddening and increase of local skin temperature when the cyanotic skin is stimulated by local trauma, by local warmth or by the subcutaneous injection of a drop of 1/3,000 histamine. A similar response follows reactive hyperaemia whereas an ulnar nerve block at the height of an attack produces only a very gradual subsidence of the cyanosis. If the mechanism of acrocyanosis were predominantly a vasomotor overaction an almost immediate relief of the signs and symptoms would be expected to follow vasomotor paralysis. But the fact that the cold, cyanotic hand may also sweat excessively does suggest at least an associated hyperactivity of the autonomic nervous system However, most investigators tend to agree that the condition is the result of an abnormal response to cold of the smaller blood vessels in the skin. An attempt has been made to place the site of the local fault in the capillary bed and venules rather than primarily in the arterioles but such a localisation is as difficult to deny as it is to prove on the available evidence. There is little doubt that more work needs to be done upon the state of the smaller veins and their contribution to the features of such vasospastic disorders as acrocyanosis and the Raynaud phenomenon.

It is stated that many patients suffering from acrocyanosis are highly strung or actually psychoneurotic and the exceptionally high incidence of the condition amongst inmates of mental institutions might be taken as support of a constitutional susceptibility indicating a generally unstable vasomotor system On closer analysis it has been shown that acrocyanosis is three times more common in mental defectives who habitually stand about, indifferent to the cold, than in any other mental disorder.[14] Such an association does not support a nervous mechanism. In fact the only constant relationship in acrocyanosis is exposure to low-grade cold, particularly when body chilling is associated The ambient temperature best calculated to reproduce the features of acrocyanosis is 15-20°C, although if the body is kept warm it is almost impossible to reproduce an attack.

In the presence of intense arteriolar spasm only a trickle of blood flows through the capillary bed into the sub-papillary venous plexuses This blood is immediately deprived of virtually all of its oxygen by the anoxic tissues and then lies stagnant to give the pathognomonic cold, cyanosis. The fact that the hand will blanch on elevation is evidence that there is little interference with the flow of blood proximal to the capillary bed. Indeed the latter and the venules may be abnormally dilated because of the dilating effect of the by-products of tissue anoxia The fact that all of the major arterial pulses are present and palpable even at the height of an attack frees the larger arteries from suspicion Until more definite data are at hand the vascular fault must be placed between the larger arteries and veins in the smaller blood vessels of the dermis—most likely the arterioles.

Pathology.—Biopsies of the skin involved in acrocyanosis have been performed and although the changes described are not remarkable, they do suggest that an advanced form of the disease is associated with more marked vascular alterations than is a mild form.[14] The most constant change is hypertrophy of the muscular medial coat of the arterioles It is impossible to tell from histological examination whether this is an organic [illegible] persistence of [illegible] local oedema [illegible] and superficia[illegible] is a fairly constant feature. This latter observation substantiates the findings of an increase in the number and size of the capillaries in the skin of the nail folds by capillary microscopy.

Whether the medial hypertrophy of the arterioles is the cause or effect of acrocyanosis is not known It may well be that chronic exposure to cold produces repeated arteriolar spasm which in the first instance is not associated with acral cyanosis. As time goes on the repeated spasm leads to the muscular hypertrophy in the susceptible individual who then develops an exaggerated cold response which becomes clinically manifest as acrocyanosis. In other words, it may not be until organic changes, however mild, have developed in the arterioles that a state of cold susceptibility sufficient to produce cyanosis develops

Clinical features.—Acrocyanosis is said to occur more commonly i young women of psychoneurotic temperament but in most large series n clear sex incidence has been noted—a feature which contrasts with Raynaud' phenomenon. The high proportion of inmates of mental institutions sufferin from acrocyanosis is associated more with lack of motion and indifference t chilling than with any functional vasomotor derangement since the conditio is several times more common in individuals who habitually stand abou *e.g.* mental defectives, katatonics.[14] In clinical practice the patient is mo frequently a lethargic individual between the ages of twenty and forty-fiv years. Almost half of the women who suffer from acrocyanosis are reporte to have chronic chilblains as well,[14] and a smaller proportion exhibit lived reticularis. We have not found the coexistence so frequently but such associa tions are not surprising since the causative mechanism in all these condition is an exaggerated vasoconstriction in response to cold.

The features of the condition are pathognomonic. The individual, mal or female, presents with the history of almost constant coldness and bluenes of the fingers and hands, less commonly of the toes and feet, for many years The cyanosis is of the glove-and-stocking type, virtually never extending abov the wrist or the mid-part of the dorsum of the foot. The discoloration i bilaterally symmetrical although the intensity usually varies on the two sides The patient complains of tightness and coldness of the fingers whose move ments are stiff and sluggish. Clumsiness in sewing, knitting and picking u fine objects is a frequent finding and is associated with a mild diminutio of the acuity of sensation. Very few patients complain of episodes of blanching Relief from the malady is obtained by artificially warming the hands, as b plunging them into warm water, or upon return to a warm environment, whe the affected parts become warm, red, somewhat swollen and, if the sense o heat and prickling is marked, quite painful. Between attacks the extremitie are nearly normal in colour but often are excessively clammy which give the impression that they are customarily, on the average, colder than the hands of an unaffected individual.

Examination of the hands confirms the cold cyanosis but the discoloratio of the skin is seldom uniform. The skin contains bright red areas—the so-called "cinnabar red spots"—and the depth of the cyanosis depends, to a large extent, upon the position of the limb, being more pronounced when it is dependent. If the skin is locally blanched by a finger pressure the pallor produced subsides slowly from the periphery only, whereas, in the normal skin, return of previous colour occurs in all parts of the area at once. Puffiness of the hands is usual and oedema, to the extent of pitting in advanced cases, may be demonstrable. Swelling is worse in the winter months when localised areas of the hands may become painful and tender and chilblains may be superimposed (Fig. 307). The palms of the hands are usually excessively sweaty even though the hand is cold. In contrast the dorsa of the hands are normally dry. Even at the height of an attack normal arterial pulsations are present at



FIG 307
Acute chilblains superimposed upon acrocyanosis.



FIG 308
Showing atrophy and disappearance of toenails on fourth and fifth toes of a long-standing case of acrocyanosis

the wrist and ankle. In severe cases cyanosis of the face, nose and ears may be encountered.

The skin shows little, if any, permanent change in uncomplicated acrocyanosis, remaining unthickened and supple, and the nails are usually normal in appearance but in long standing cases they may atrophy (Fig. 308). The



FIG. 309
Gangrere of toes with loss of toenails and atrophy of pulp tissue in a sixty-seven year old woman with a life-long history of acrocyanosis. There was no major arterial disease or diabetes

shiny, tight appearance of the skin in severe cases is the result of the associated swelling, and disappears with its relief. Paresis, ulceration or contracture are rare although some delay in the healing of cuts and septic lesions, to which the fingers become prone in the winter months, is the rule. When frank ulceration or gangrene occur some suspicion must be placed upon the diagnosis of pure acrocyanosis and the coexistence of organic vascular disease with the acral cyanosis must be considered. We have had only two cases of peripheral gangrene which could be attributed to acrocyanosis alone (Figs 309 and 310). Generally speaking acrocyanosis causes little disability and does not seriously affect the general health of the individual or the integrity of the extremities. It persists for many years and may lessen in intensity in the later years of life.



FIG. 310
X-ray of the toes showing osteoporosis and phalangeal bone destruction

Treatment.—The first principle in the management of acrocyanosis is to maintain the local circulation by avoiding exposure of not only the hands but

also the body to long periods of cold and damp. The body should be warmly clad and the hands covered with woollen mittens or fur-lined gloves when the patient is out-of-doors For the feet, thick woollen stockings and fur-lined, rubber-soled boots, which are damp-proof, should be worn and the patient should be encouraged to walk briskly and not stand about. The temperature of the rooms in his or her home should be kept between 24 and 25°C. if possible It is probably this environmental factor which makes acrocyanosis a relatively uncommon condition in North America, where some form of central heating is almost universal. If the patient is thin a more liberal weight-gaining diet may be prescribed and in severe cases the patient may be advised to winter, or reside permanently, in a dry, warm climate where possible.

In severe cases sympathectomy may be advised but, on the whole, the results are disappointing, an additional argument against the primary seat of the malady being the sympathetic nervous system. If local and body chilling is avoided after sympathectomy the improvement may be considerable but the initial vasodilatation is not maintained and after an early period of substantial improvement the symptoms tend to recur although seldom as severely as previously It is probable that a good deal of the final improvement results from the abolition of sweating which in itself, by preventing excessive evaporation, is advantageous, for it helps to keep the part warm. Generally speaking the results of sympathectomy are as good as those obtained in Raynaud's phenomenon since the benefit in both conditions depends upon the degree of digital artery obliteration.

There have been favourable reports of temporary benefit from hyalase iontophoresis This procedure is said to reduce the local swelling and render the hands less stiff and more comfortable. Its greatest usefulness is as a temporary measure in the relief of the severe case We have had no experience of this form of treatment

CHILBLAINS

Chilblains, the pernio syndrome, perniosis, erythrocyanosis, erythrocyanosis frigida, erythrocyanosis crurum puellarum, nodular vasculitis, erythema induratum, Bazin's disease and dermatitis hiemalis are a few of the terms which have been applied to various stages in the progress of a single disease entity There has been a studied attempt, to which the above terms bear witness, to break up the condition, which we propose to [illegible] **chilblains,** into a [illegible] virtue nor c[illegible] of the skin [illegible] term to use [illegible] most logical [illegible] The common factor in chilblains and all the conditions bearing the synonyms listed above [illegible] skin [illegible] ise [illegible] th[illegible] subcutaneous nodules and, in [illegible] and advanced stages, painful and indolent ulceration The

underlying tissue pathology in chilblains has a vein of similarity throughout but the stage at which biopsy is performed, and interpreted, has influenced different investigators in the past to attempt to divide the conditions into specific entities. It must be reiterated that the modes of response of the skin and of the subcutaneous tissues to irritants are definitely limited so that it is not wise to place too much reliance on the histology in separating, into artificial compartments, the stages of a single disease entity, stages which on clinical as well as histological grounds are, for all practical purpose, impossible to differentiate.

Chilblains are common in countries where individuals are exposed for long periods to low-grade cold and damp. For this reason it is quite common in England in contrast to North America although reports suggest a rising incidence there in response to fashions.[11] In the early and acute stages chilblains are seasonal, appearing with cold weather and disappearing with warm weather, and reversible, but with repeated and chronic exposure permanent tissue alterations develop and the lesions no longer clear up with the advent of summer weather. Once ulceration becomes established it is prone to persist in some degree all the year round. It is best to divide the condition into two stages, an acute stage which is reversible and a chronic stage in which permanent tissue changes are present and in which ulceration may or may not have developed. In this stage chilblains are never completely reversible since the tissue changes have progressed beyond the functional to the organic

Acute chilblains.—The acute phase of chilblains differs very little from the first stage of frostbite and resembles, symptomatically, the hyperaemic stage of immersion foot. In the past the lesions were most frequently encountered on the exposed face and backs of the hands, particularly the little finger, and were rarer on the legs and feet which were well covered.[3] Nowadays it is almost exclusively encountered on the legs and feet of women who wear short skirts, thin stockings and footwear which is inadequate protection from cold and damp Not infrequently, however, there are associated chilblains on the hands. Although they may occur at any age and in either sex, more than three-quarters of the patients are under the age of twenty years[3] with the highest incidence in the adolescent female.

With the onset of cold weather the ill-clad extremities begin to burn and itch and if examined at this stage the skin is red or cyanotic and cold and the part is slightly swollen. Blebs of varying size with well-defined margins and a dusky colour may develop if exposure is prolonged. The disease at this stage often presents a striking resemblance to herpes. The lesions are usually bilaterally symmetrical and in some instances the vesicles are haemorrhagic (Fig, 307). On coming in from the cold upon exposure to warmth the itching and burning become intensified with a sense of formication Too rapid warming as by placing the extremities near an open fire or in hot water may produce vesicles not previously present

The acute stage is fully developed within eighteen to twenty-four hours of the initial exposure and lasts only a few days if the exposure to cold is not repeated. In seven to fourteen days there is no evidence of the chilblains unless haemorrhagic blebs have occurred, in which case rupture is usual with the development of a superficial, weeping patch like raw ham. This patch fades to a brownish hue which persists covered by a thin layer of adherent scales (Fig. 311). Similarly, if the blisters become infected or the skin burned or



Fig. 311
Healing stage of acute chilblains of the toes.
(*Surgery, Gynecology and Obstetrics*.)

broken by exposure to heat or to vigorous massage during the recovery period, convalescence is prolonged. Recovery is complete after the first attack unless the exposure is repeated, when the condition usually progresses to the chronic stage with permanent discoloration, nodule formation and finally ulceration of the skin.

The mechanism of acute chilblains is severe local vasospasm of the blood vessels of the skin of a susceptible individual upon exposure to cold and damp. Since not everyone develops chilblains an individual suspectibility, as yet of unknown nature, must be postulated. In the first instance the vasospasm is reversible since organic vascular and tissue changes of a permanent nature are not present. Biopsy at this stage reveals a non-specific inflammatory reaction with transudation of serum and perivascular infiltration of the small vessels in the papillary layer of the cutis.[5] That a certain immunity may develop is manifest by the spontaneous recovery that may occur after the age of twenty years. Girls sometimes cease to suffer from attacks after marriage. Sometimes after suffering in their youth a period of immunity develops only to be followed by a recurrence of symptoms in middle age. This is a not uncommon sequence of events, whose relationship to each other may not be observed if the initial trouble in adolescence has been forgotten.

In the acute stage avoidance of further exposure of the limbs to cold and the provision of a warm environment and adequate clothing to protect

the affected parts and to prevent body chilling will ensure no further attacks. If blisters are present they should be treated by the "exposure" method and not pricked. Excessive heat, massage and local applications are best avoided but systemic antibiotics may be exhibited if there is significant secondary infection of the blisters. If precautions against cold are rigidly followed no further trouble should occur; if not, repeated and prolonged cooling will lead ultimately to irreversible changes in the exposed parts and the chronic stage becomes established perhaps because recurrent untreated vascular spasm leads to the development of organic changes in the affected vessels.



FIG. 312
Classical chronic chilblains in the wasted leg of a thirty year old woman who had poliomyelitis as a child. The other leg was normal

Chronic chilblains.—It is this stage of chilblains which has led to the greatest controversy, and to repeated attempts to separate into clinical entities different stages in the downhill course to irreversibility.[12] A factor common to all these entities is sensitivity to prolonged low-grade cold and differences depend upon the duration of exposure, the individual susceptibility of the tissues, and the stage at which the patient seeks medical advice. It must be appreciated that histologically skin and subcutaneous tissues, including blood vessels, can respond to noxious agents in but a limited fashion. For this reason the histology is found to be remarkably constant in all the conditions we group together as chronic chilblains, regardless of the name that has been applied to them.

It is generally agreed that prolonged cooling of the extremities requires in addition some as yet obscure background of vascular susceptibility to explain the development of the full clinical picture.[7, 8, 16] In short, the "soil" in the limb must be defective. Seldom can the defect in the tissues be ascertained but there is no doubt that a previous attack of anterior poliomyelitis renders a limb unduly susceptible to the effects of cold (Fig. 312). Excessive fat in the legs is a predisposing factor probably because fat is a poorly vascularised tissue and being poorly nourished is more susceptible to injury and to the local effects of cold. An additional point may be that the physical state of fat in the tissues requires a constant temperature which is not maintained in these susceptible individuals. Excessive deposits of fat may be associated

with the pubertal and the menopausal states so that it is not surprising that attempts have been made to describe the chronic chilblains occurring at these two stages of life as separate clinical entities. When ulceration develops in the final stage of the condition tuberculosis has been suggested to be a causative agent. Like other authors,[11, 15] we have never been able to demonstrate, or culture, directly or by guinea pig inoculation, tubercle bacilli from any lesion biopsied Had we done so we would have ceased to regard the condition as a vascular entity and would have considered it a cutaneous tuberculide. When tuberculosis or other general disease is present the skin lesion is probably not essentially tuberculous but rather coexistent chilblains that have developed as a consequence of reduced general health and resistance.[5]

In the final analysis chronic chilblains are simply a manifestation of a chronic obliterating vascular disease of the smaller arteries of the skin and subcutaneous tissues (Fig 317). According to the degree of obliteration, and therefore anoxaemia, there is first cutaneous discoloration, followed by necrotic, nodule formation and finally overt ulceration. It is in such final stages that vascular obliteration and tissue damage have reached a degree of permanency from which reversibility is no longer possible. So long as cutaneous ulceration is absent or slight the condition assumes the clinical appearance of nodular vasculitis, erythrocyanosis and erythrocyanosis frigida (crurum puellarum). Once cutaneous ulceration is fully established it tends to progress to what has been described as erythema induratum and Bazin's disease. There is no further virtue in retaining more than the simplest of the many terms attached to the condition, and the term we propose to retain is chilblains which means a blotching of the skin with or without ulceration, resulting from cold[10]

Clinical features.—All too often in taking the history of patients with chronic chilblains exposure to damp cold is overlooked or if obtained is not considered relevant to the condition with which the patient presents. Close enquiry will reveal that the patient has had trouble with her limbs since an early age and an actual history of acute chilblains will be elicited in a high proportion of cases A seasonal incidence is virtually always found, there being exacerbation in the winter months and regression in the summer[3, 8, 14, 15] The condition is almost entirely confined to women, with two peaks of frequency —puberty to twenty-five years and from thirty-five years to the menopause. Old people are rarely affected

In the young woman it is a disease of fashion and no better description of the precipitating factor can be given than that of Lewis.[8] "It came in with short skirts and thin stockings and will go out with them." The young women who have the disease frequently have stout legs and thick ankles but these are by no means universal, as they are in women who develop the condition in later years After the initial acute attack, or after several

years of the chronic form, an apparent resistance to cold may develop and the condition may clear up either never to return or to return only with middle age. The age at which spontaneous remission may develop is twenty to twenty-five years and has coincided with marriage in a number of cases as well as with the wearing of more sensible clothing.

In the older woman fashions appear to be less at fault than the tissues themselves. These women are nearly all of a stout, florid build with fat legs and thick ankles. Such an excess of fat is often present in a limb which has been the seat of poliomyelitis and is known to be prone to develop acute and chronic chilblains.[17] In both cases the poorly vascularised fat is abnormally susceptible to the chronic vasoconstricting effects of cold and damp. The majority of women in the older age group—thirty-five years to the menopause—give a life-long history of cold limbs and have had acute chilblains in the past from which they have recovered, only to have the symptoms return with increasing age, adiposity and the reduced activity and metabolism of advancing years. In both age groups the condition is commoner when a general disease, *i.e.* tuberculosis or heart disease, is present to lower the patient's resistance. The higher incidence amongst the poorer classes is an expression of poorer nutrition and an inability of poor people to keep themselves and their environment sufficiently warm.

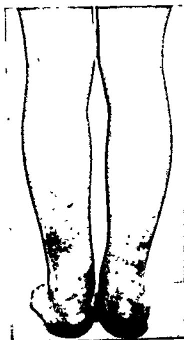


FIG. 313

Early stage of chronic chilblains in a thirty year old woman with a twelve year history Note the thick ankles, prominent hair follicles, and pigmentation

(*Surgery Gynecology and Obstetrics*)

It will be recognised by now that chilblains are open to pursue one of several courses. First, after one or more acute attacks, the condition may disappear never to return or it may return seasonally for several years and then never come back after the age of twenty years or so. Secondly, after an apparent disappearance, chilblains may recur again in early middle age, and either recur perennially until after the menopause or progress rapidly to ulceration. Finally, in some young women the condition begins with puberty and progresses inexorably to frank ulceration with no evidence of healing or remission even in summer.

In the early stages of the chronic disease the most striking aspect is blotchy discoloration of the skin of exposed areas, chiefly the lower third of the legs, around the malleoli and rarely the dorsa of the feet and the legs up to the knees, in cold weather (Fig 313). It is usually bilaterally symmetrical although often more severe on one side than the other. The patches are dusky, reddish-purple blotches from which the colour can be blanched by

The outline is diffuse and fades into the surrounding skin pressure (Fig. 314) The outline is diffuse and fades into the surrounding skin ... the touch, redder than is normal and contains prominent hair ... skin may

... it is for cosmetic reasons that most young ... advice With the advent of warm weather rapid recovery occurs and the legs assume an almost normal appearance and colour. In a small proportion of cases the legs are uncomfortably warm and ache in warm weather, particularly when the patient has been on them a lot.



Fig 314
Non-ulcerated chronic chilblains

After several winters the disease may regress never to return or the discoloured patches may become larger, swollen, resistant and nodular. The nodules are elevated above the surface of the skin, to which they are attached, and are firm, painful and tender to the touch, varying in size from a few mms. to several cms in diameter. Most frequent in the lower third of the legs just above the ankles, they may occur on the calves of the legs, around the knees, on the buttocks and also over the triceps brachii. At first the nodules appear only in the cold weather, last for several weeks and then almost disappear when warm weather comes They never completely regress since if the limb is carefully palpated the subcutaneous thickenings can be appreciated even when the overlying skin seems healthy. After a few years the nodules are obviously persisting throughout the summer months and it is at this stage that breakdown and ulceration commences. Actual breakdown is usually preceded by a period of itching and a small, painful, violaceous

blister develops, to be followed by *rupture, ulceration* and relief of pain The ulcers occur in successive crops which tend to heal after several weeks, or months, disappearing *completely* in late spring or early summer but leaving a *permanently pigmented scar* over which the skin is shiny and atrophic, covered with fine scales and possessing an unhealthy tendency to recurrent ulceration.



FIG. 315
Advanced stage of chronic chilblains in a twenty-four year old woman with a ten year history of chilblains Picture taken after one week of bed rest and bradasol dressings.
(*Surgery, Gynecology and Obstetrics*.)

If the condition continues to progress the ulcers become larger, coalesce and eventually they no longer heal with the *advent of* warm weather but remain open all year round, with some diminution in size in the summer months (Fig 315). It is this stage of chronic chilblains which has been termed Bazin's disease and erythema induratum by some authors whose opinion is that a certain proportion of *these patients* are *suffering* from an ulcerative form of cutaneous tuberculosis In our opinion the ulcerating stage of chronic *chilblains is not tuberculous.* Bazin's original description[1] of the condition would pass for most of the synonyms that have been applied at later dates and, finally, *it is difficult to visualise a tuber*culous lesion that occurs in the winter and heals, sometimes completely, in the summer without treatment. Bazin included no histological sections in his study so that any comparisons with tuberculide must be accepted with reserve and subsequent descriptions of "*tubercles*" and giant cell systems are consonant with fat necrosis.

In long-standing cases of chronic chilblains the legs, which are often stout and thick to begin with, become permanently swollen by a firm, *resistant infiltration of the subcutaneous tissues.* There is residual brownish pigmentation with disfiguring atrophic scars surrounded by skin which contains enlarged, pigmented hair follicles from which the hairs are usually absent (Fig. 315). Almost half of the women with chronic chilblains are said to have acrocyanosis[14] and a smaller proportion have an associated livedo reticularis, but in our experience neither association is frequent. The skin in the supramalleolar region of the legs feels abnormally cold and by skin temperature readings it can be shown that this region of the leg does not warm up as well after lumbar sympathectomy as does a limb not so affected. All of the major pulses are palpable at the ankle and we have found no major arterial disease by arteriography

Careful general examination must be carried out to exclude systemic diseases although these are seldom associated. In the past it was noted that chilblains were more common in people with heart disease and tuberculosis[3] but this is not so today. Hypertension is said to be a frequent accompaniment[6] but only three of more than eighty patients seen by the authors have had a raised blood pressure. Positive tuberculin reactions have been reported in as high as 85 per cent of patients with chronic chilblains, but it is doubtful that this is any higher than that in a normal ward population in this country were all patients tested. A history of or the presence of healed tuberculous lesions is no higher than in patients presenting with quite dissimilar conditions. When tuberculosis coexists with ulcerating lesions of the legs the association is no more than coincidental since tubercle bacilli are rarely, if ever, demonstrable in the cutaneous ulcers Disturbance of general health is associated with an increased incidence of chronic chilblains by no other connective relationship than the reduction of the patient's general health and resistance to cold which they occasion.

PATHOLOGY—It cannot be overstated that there is no pathognomonic microscopical picture specific for this condition and if a close study is made, by serial sections, of a lesion, the changes said to be characteristic of "erythema induratum," "nodular vasculitis" and "Bazin's disease" can all be demonstrated in the one limb Telford has stated that unlabelled sections of the above could not be distinguished, in the absence of the clinical picture, from fat necrosis of the breast if breast tissue is excluded from the section[13] In short the histological picture is characterised by its non-specificity. The mechanism underlying the development of these tissue changes appears to be repeated vasospastic attacks which produce, at first, recurrent anoxaemia in the skin and subcutaneous tissues of the legs. With the progress of time the functional changes in the blood vessels become organic alterations so that recurrent anoxaemia gives way to chronic ischaemia with incomplete recovery of the circulation between attacks. At this stage organic tissue damage develops to be followed by attempts at repair. The picture has superimposed upon it a degree of inflammatory reaction proportional to the extent and the chronicity of ulceration. The preponderance of the lesions in the lower third of the legs is probably an exaggerated expression of the normally poor blood supply to this part of the body[2] which consists almost entirely of avascular tendon and bone and is exposed to the full effects of gravity and environment

The dominating feature in all sections, whether of a nodule or an ulcerating lesion, is necrosis of fat with a secondary reaction largely an effect of irritating free fatty acids The nodule is really the reparative stage of fat necrosis complicated by a lesser or greater degree of inflammatory reaction. In the adjoining tissues there may be numerous giant cells of the foreign

blister develops, to be followed by rupture, ulceration and relief of pain. The ulcers occur in successive crops which tend to heal after several weeks, or months, disappearing completely in late spring or early summer but leaving a permanently pigmented scar over which the skin is shiny and atrophic, covered with fine scales and possessing an unhealthy tendency to recurrent ulceration.



Fig. 315
Advanced stage of chronic chilblains in a twenty-four year old woman with a ten year history of chilblains. Picture taken after one week of bed rest and bradasol dressings
(*Surgery, Gynecology and Obstetrics*.)

If the condition continues to progress the ulcers become larger, coalesce and eventually they no longer heal with the advent of warm weather but remain open all year round, with some diminution in *size in the summer months* (Fig 315). It is this stage of chronic chilblains which has been termed Bazin's disease and erythema induratum by some authors whose opinion is that a certain proportion of these patients are suffering from an ulcerative form of cutaneous tuberculosis. In *our opinion the ulcerating stage of chronic* chilblains is not tuberculous. Bazin's original description[1] of the condition would pass for most of the synonyms that have been applied at later dates and, *finally, it is difficult to visualise a tuber*culous lesion that occurs in the winter and heals, sometimes completely, *in the sum*mer without treatment. Bazin included no histological sections in his study so that any comparisons with tuberculide *must be accepted with reserve and subsequent descriptions of* " tubercles " and giant cell systems are consonant with fat necrosis.

In long-standing cases of chronic chilblains the legs, which are often stout and thick to begin with, become permanently swollen by a firm, resistant infiltration of the subcutaneous tissues. There is residual brownish pigmentation with disfiguring atrophic scars surrounded by skin which contains enlarged, pigmented hair follicles from which the hairs are usually absent (Fig. 315). *Almost half of the women with chronic chilblains* are said to have acrocyanosis[14] and a smaller proportion have an associated livedo reticularis, but in our experience neither association is frequent. The skin *in the supra*malleolar region of the legs feels abnormally cold and by skin temperature readings it can be shown that this region of the leg does not warm up as well after lumbar sympathectomy as does a limb not so affected. All of the major pulses are palpable at the ankle and we have found no major arterial disease by arteriography.



FIG. 317

A—Biopsy section from an ulcer of the leg of a nineteen

(Surgery, Gynecology and Obstetrics.)

body type usually swollen by fat (Fig. 316). Surrounding the nodule and most concentrated at the periphery of the necrosed area are lymphocytes, fibroblasts and granulation tissue. The activity and degree of the inflammatory reaction is largely proportional to the extent and duration of ulceration. The picture is completed by a variable degree of obliterating endarteritis which has been termed an "angiitis" by some authors.[11] The latter term is not strictly accurate because the blood vessel walls are rarely infiltrated with



FIG. 316

Numerous "tubercle-like" nodules with central caseation, giant cells, epithelioid cells, and lymphocytes. Biopsy is from the patient whose legs are shown in Figure 315. Culture and guinea pig inoculation from the other half of this biopsy were negative. Haematoxylin and eosin, ×40. (*Surgery, Gynecology and Obstetrics.*)

inflammatory cells but more usually "cuffed" by them. The blood vessels are thickened in all three coats with intimal proliferation and muscular hypertrophy predominating. The vascular reaction is mainly perivascular, and may extend to the veins, with an infiltration chiefly of lymphocytes and plasma cells although occasionally with considerable numbers of leucocytes too. In some instances the endarteritis may be so advanced that the lumen of the smaller arteries is completely obliterated (Fig. 317). In short the above picture is that of necrosis and liquefaction of fat surrounded by a macrophage response and a chronic inflammatory reaction representing the response of the tissues to the irritation of the fatty acids released by hydrolysis of the fat and secondary infection from ulceration of the skin. With very little, if any, alteration this histological description would fit that of fat necrosis as seen in the breast[4] or systemic nodular panniculitis[13] (Fig. 318). If numerous sections are taken from a single biopsy or from several lesions on the same limb several variations of this basic picture will be noted depending upon the age of the lesion, the presence or absence of ulceration, and so of secondary inflammation, and the stage of repair. Thus there may be extensive fibrosis of the

The inguinal lymph nodes are usually enlarged, firm and shotty, particularly when ulceration is present on the leg. Biopsy has never shown more than sinus hyperplasia and fibrosis compatible with chronic inflammation somewhere in the territory which the affected nodes drain (Fig. 319).



FIG. 319

Lymph node from the groin of the patient shown in Figure 315 and whose biopsy sections are shown in Figure 316 (*Surgery, Gynecology and Obstetrics.*)

TREATMENT.—There is no specific treatment for chronic chilblains except prophylaxis. It is important therefore that an individual who has shown an abnormal response to the effects of cold and damp avoid undue exposure to the inimical environment and, when exposure is unavoidable, to make sure that the limbs and the body are adequately protected by woollen stockings and warm, wet-proof footwear to prevent local cooling and by plenty of warm clothing to prevent body chilling. In those who can afford the luxury, temporary or permanent residence in a warm, dry climate may be advised. The temperature of the patient's home should be kept in the neighbourhood of 24 to 25° C.

Local treatment is seldom of much benefit and local applications are best avoided. In severe cases with painful ulceration a period of bed rest with elevation of limbs will relieve the cyanosis and swelling. Care should be taken to avoid excessive warmth as it may lead to an exacerbation of the pain. Should it be necessary to apply a medicament to the legs to prevent them from sticking to the bed clothes or dressings, 1/2,000 Bradosol is efficacious and non-irritating. Ulcers may
be inoculated into a guinea
bacilli are never present
compresses and Bradasol the appropriate antibiotic is administered systemically. We have given streptomycin and isonicotinic acid hydrazide empirically to a number of patients with no greater success than the conservative measures

subcutaneous fat rather than active saponification of fat with predominant giant cells. Vascular changes approaching obliteration may be present in one region while in another perivascular infiltration is the striking feature. Occasionally a small artery is completely replaced by a granulomatous "*pseudotubercle*" (Fig. 317). We have never been able to demonstrate



FIG. 318

A and B—Sections from two patients suffering from fat necrosis of the breast If it were not for the presence of a recognisable breast tissue in other fields of these sections they would be indistinguishable from chronic chilblains Haematoxylin and eosin, × 40

(*Surgery Gynecology and Obstetrics*)

tubercle bacilli by culture or by guinea pig inoculation. This experience is in accord with that of others.[11, 15] The basis for incriminating tuberculosis in these ulcerating lesions of chronic chilblains is founded on most tenuous ground and it should, along with attempts to dissect a single disease into several clinical entities, be dropped forthwith.

The inguinal lymph nodes are usually enlarged, firm and shotty, particularly when ulceration is present on the leg. Biopsy has never shown more than sinus hyperplasia and fibrosis compatible with chronic inflammation somewhere in the territory which the affected nodes drain (Fig 319).

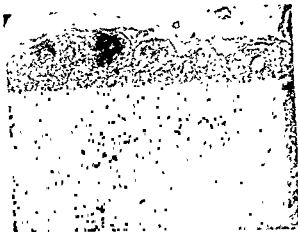


Fig. 319

Lymph node from the groin of the patient shown in Figure 315 and whose biopsy sections are shown in Figure 316 (*Surgery, Gynecology and Obstetrics.*)

Treatment.—There is no specific treatment for chronic chilblains except prophylaxis It is important therefore that an individual who has shown an abnormal response to the effects of cold and damp avoid undue exposure to the inimical environment and, when exposure is unavoidable, to make sure that the limbs and the body are adequately protected by woollen stockings and warm, wet-proof footwear to prevent local cooling and by plenty of warm clothing to prevent body chilling. In those who can afford the luxury, temporary or permanent residence in a warm, dry climate may be advised. The temperature of the patient's home should be kept in the neighbourhood of 24 to 25°C

Local treatment is seldom of much benefit and local applications are best avoided In severe cases with painful ulceration a period of bed rest with elevation of limbs will relieve the cyanosis and swelling Care should be taken to avoid excessive warmth as it may lead to [illegible]

[illegible] ...culous and ... may be biopsied and cultured and biopsy material may be inoculated into a guinea pig. Secondary infection is common but tubercle bacilli are never present. If the secondary infection does not respond to compresses and Bradasol the appropriate ant[illegible] cally We h[illegible]

described. Mecholyl and hyalase iontophoresis have been followed by substantial local improvement in a number of earlier cases, but such measures are strictly of temporary benefit. It would seem that sympathetic denervation of the affected limb would be the logical approach to relieve the chronic arteriolar vasospasm predominantly responsible for the condition. We have performed lumbar sympathectomy on more than fifty patients suffering from the chronic chilblain phenomenon. The subjective improvement has in some been considerable even though the limb has been objectively little changed. The sense of coldness, burning and heaviness is usually relieved but the thickness of the limb and the colour changes remain much the same as before with scaly, atrophic areas where there was previously ulceration (Fig. 320). This is not surprising since the essential fault is a local vascular instability, and sympathectomy cannot materially influence an intrinsic fault. The objective results are much the same as those obtained in "Raynaud's Disease" where too the degree of improvement is proportional to the degree of small artery obliteration. Prophylactic measures as protection against cold by warm clothing and warm environment must be continued even after sympathectomy. If this is strictly adhered to some remarkable cures of ulceration will be obtained and maintained. In some long-standing cases residual oedema of the legs may be troublesome and in these well-fitted one-way stretch elastic stockings should be worn to control the swelling.



FIG. 320
The same patient as shown in Figure 315, two years after bilateral lumbar sympathectomy. Pigmentation persists and scaly, atrophic skin covers the sites of previous ulceration
(*Surgery, Gynecology and Obstetrics*)

R. B. L.

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CHAPTER XVII

VASOMOTOR AND SUDOMOTOR DISORDERS

THE term "vasomotor disorder" has been loosely applied in the past and many conditions have been attributed solely or in part to vasomotor dysfunction for little reason other than convenience of classification. Strictly speaking the term "vasomotor disorder" should designate a disease or syndrome in which a change in the circulation of the limb results from a functional disturbance of the vasomotor supply to that limb. If this strict definition is adhered to many of the disorders to be discussed below must be omitted. However, it has been felt that there exists a group of conditions, the basic mechanism of which is ill-understood but which are accompanied by clinical, and sometimes laboratory, evidence of dysfunction of the central or peripheral autonomic nervous system. Perhaps the best example of a purely central malfunction of the autonomic nervous system is essential hyperidrosis while the best examples of peripheral malfunction are the vascular paralyses following sympathetic and peripheral nerve section. Between these fall a group of poorly understood conditions, such as causalgia and erythralgia, which have a definite though perhaps secondary vasomotor component. Finally there are those spontaneous variations in vasomotor activity which are important in the regulation of body temperature in response to environment, sleep, food, exercise and changes in posture. These play an important part in the maintenance of the "milieu interne" of the body and are not within the scope of this chapter.

VASOMOTOR ABERRATIONS AFTER SYMPATHECTOMY

The vasomotor changes which follow loss of sympathetic innervation, usually as a consequence of surgical intervention, have been discussed fully in Chapter III It remains to mention briefly those rare cases in which vasomotor tone is very slowly and inadequately regained after sympathectomy This does not occur, to our knowledge, in the upper extremities When failure to regain vasomotor tone occurs an erythralgic-like state develops in the feet which become exceedingly hot, burning and painful [10, 34] The patient complains that his feet feel like "hot plates" and in order to get rest he may sleep with them outside of the bed clothes. If the peripheral blood flows are estimated they are found to be persistently high, being maintained at the level commonly found only in the first forty-eight hours following sympathectomy There is no treatment for the condition which tends to improve spontaneously with the passage of time

VASOMOTOR DISORDERS AFTER PERIPHERAL NERVE SECTION[30]

The peripheral nerves to the limbs are mixed in function and when one is divided there is not only loss of movement and sensation in the territory of the sectioned nerve but also an immediate vasodilatation due to interruption of the sympathetic vasoconstrictor fibres which run in it. This leads to the "**warm phase**" consisting of full vasodilatation, in which the skin is red and dry and the superficial veins dilated. The picture is the same as that seen after sympathetic denervation. Although there is no precisely clear-cut duration for this phase a rapid restoration of vascular tone in the denervated territory occurs just as after sympathectomy. However, instead of a steady stable state being maintained as it usually is after sympathectomy there is a kind of overshoot and the skin in the affected region, especially that of the digits, becomes markedly and permanently colder than the normal parts of the extremity. This "**cold phase,**" in which the temperature of the part corresponds roughly to that of its environment, begins usually within two to three weeks of the original injury although its onset may be delayed for several months. In cases where the "warm phase" persists for several months the denervation of the limb has usually been extensive or complete as in brachial plexus lesions for example.

Once the "cold phase" is established the skin in the denervated area loses its independence of environmental changes of temperature and acts like an inert body. The blood supply is regulated by the needs of local tissue metabolism as dictated by the environment and is no longer influenced by active movement which may be absent or greatly diminished. The factors responsible for the "cold phase" cannot be so easily explained as can those responsible for the "warm phase." It is well known that the blood vessels in a sympathectomised limb are abnormally sensitive to circulating adrenaline. Although this is of no practical importance in the recovery of tone following sympathectomy or in the recurrence of Raynaud's phenomenon after sympathectomy it may be important in peripheral nerve section. The most likely explanation of the "cold phase" may be that the axon reflex, an important factor in producing the vascular reactions responsible for maintaining skin temperature in normally innervated limbs, is abolished. Perhaps inactivity of the part alone, the loss of the power of movement, is responsible for the paralysed limb assuming the temperature of its environment. The loss of reaction holds for all stimuli, including cold and trauma, and may be an important factor in the occurrence of the trophic lesions not infrequent in denervated extremities. The fact that normal warmth does not return to the denervated territory until the sensory fibres have regenerated, at which time the axon reflex has been restored, points to the importance of loss of the axon reflex in the development of the "cold phase" Until the nerve has regenerated the skin temperature and blood flow of the denervated limb

will not respond to indirect body heating but only to conditions which alter the local metabolic needs of the part, *i.e.* reactive hyperaemia.

Vasomotor changes of a similar character develop after anterior poliomyelitis in the late paralytic stage. Although the conditions in the limb resemble the "cold phase" after peripheral nerve section the blood flow to the part can be raised to almost a full vasodilatation level by indirect body heating It is probable that the vascular state here is more the result of disuse and loss of assistance to the circulation by voluntary muscle activity than it is of antero-lateral horn damage. In such limbs the skin becomes cyanotic, cold and abnormally susceptible to the effects of local cold so that chronic chilblains are a frequent complication Sympathectomy usually produces considerable improvement of the circulation in such a limb. The treatment of the "cold phase" which follows peripheral nerve section is repair of the divided nerve, since recovery of vasomotor control will return only when the function of the nerve is restored.

SUDECK'S ATROPHY

The post-traumatic osteoporosis of Sudeck,[17] also known as post-traumatic reflex dystrophy, acute atrophy of bone, peripheral trophoneurosis, reflex nervous dystrophy and minor causalgia,[9] is an acute atrophy of the bones of a limb coming on after a usually minor injury and accompanied by signs and symptoms of vasomotor over-activity There is usually a history of minor trauma to the affected part of the limb. The ankle is the site of predilection, followed by the wrist The most frequent precipitating injury is an almost-forgotten "sprain," in fact approximately 5 per cent of all sprains will be followed by some degree of Sudeck's atrophy [17]

Over a period of weeks following the injury pain, local heat, swelling and tenderness develop The pain is burning in type with paroxysmal exacerbations exaggerated by movement so that there is eventually a considerable component of disuse superimposed. Oedema is constantly present being localised around the injured joint but it may be more extensive and associated with considerable chronic oedema of the limb. The extremity is warm, oscillations are increased and peripheral blood flow is reported to be elevated [17] The muscles may be hypertonic, attempting to splint the joint. The early phase of vasodilatation gradually gives way to one in which the limb is cold, cyanotic and wasted. Colour changes may be intermittent as in Raynaud's phenomenon and the limb may be excessively sweaty. X-rays reveal a variable degree of spotty decalcification of the bones of the affected part, usually the ankle or wrist (Fig 321) At first spotty, the osteoporosis later becomes diffuse probably because of superimposed disuse atrophy. In the first instance the decalcification is due to hyperaemia since it is too rapid and too advanced to be attributed to disuse alone. There may in fact be advanced osteoporosis while the joint is still in active use. Biopsy of the bones has shown marked osteoblastic activity and increased vascularity in the acute phase

whereas in the late stages there is no such bone reaction, the appearances being indistinguishable pathologically from those of disuse atrophy.

The condition seems to be the result of vasomotor reflexes beginning in the injured tissues and passing by somatic sensory nerves to higher centres whence vasodilator reflexes are initiated. It is impossible to identify accurately



Fig. 321
Radiograph of the hand Spotty atrophy of Sudek

the efferent course of the vasodilator stimuli so initiated but they may be sympathetic reflexes, spinal reflexes or axon reflexes. *The fact that the pain* and vasodilatation often do not follow a neurological pattern suggests that *the effects may be the result of vasodilator* substances produced at the end organs. In the first stages there is vasodilatation but this is not maintained, giving way to vasospasm not unlike that of Raynaud's phenomenon. The unilateral nature of the condition and the history of trauma should make the diagnosis clear.

Mild cases often subside in a few weeks spontaneously or after treatment. In more severe cases, particularly if not vigorously treated, residual deformity, joint stiffness and even contractures may result. If osteoporosis is advanced fracture of the bones may complicate the disease. The severity of the original injury does not govern the eventual course; in fact severe injuries are seldom followed by Sudeck's atrophy. For this reason a patient may be suspected of malingering if the examiner is not aware that this condition may complicate such minor injuries as "sprains".

With the above knowledge at hand it is apparent that the best form of treatment is preventive in that all sprains must be treated adequately from the outset. This is best done by strict immobilisation of the affected joint, weight bearing and encouragement of active movement of the other joints of the affected limb. If such measures are adopted this complication of the inadequate treatment of "sprains" and minor subluxations will be avoided. Should Sudeck's atrophy become established, early recognition of the complication is necessary so that pain can be relieved and the reflex responsible for the hyperaemia can be depressed or interrupted as soon as possible. At first conservative measures such as relief of pain, paravertebral blocks to interrupt reflex arcs and physiotherapy in the form of gentle heat and massage to the part with encouragement to move the joint to the point of tolerance are recommended. Should these be ineffective, immobilisation in plaster may give relief but if used for the ankle it must be a "walking plaster" so that the rest of the limb does not develop the effects of disuse. Most patients recover with the above conservative measures even though X-ray of the affected part may show little or no improvement in the texture of the bones when clinical [illegible]

symp[illegible] The results will be best when a prior paravertebral block has shown relief of symptoms over a period of some hours. It is difficult to explain why sympathectomy should produce good results, and in many a lasting cure, when vasodilatation is in fact a feature of Sudeck's atrophy. It may be that the vasodilatation is caused by the pain and the sympathectomy has interrupted pain fibres travelling in the sympathetic nerves. Whether such nerves exist or not is still controversial.[15, 5] Another possibility is that the condition is caused by pain-producing metabolites liberated by the efferent stimuli and that sympathectomy relieves the pain by increasing the circulation and washing away these substances. Whatever the mechanism it is a fact that sympathetic denervation is followed by a high proportion of lasting cures in Sudeck's atrophy which has not responded to more conservative measures.[24]

CAUSALGIA

Causalgia is the term used to describe the burning pain and vasodilatation which follow, on rare occasions, partial division or bruising of a nerve or

involvement of a nerve in the scar tissue of a wound.[21] Median nerve injury is responsible for the vast majority of all cases but the condition may occur in the territory of the sciatic nerve or any other peripheral nerve. Not uncommonly the digital nerves, injured when a finger has been cut, crushed, bruised or lacerated, and amputation stumps, are affected. It is thought that the marked concentration of vasomotor nerve fibres in the median nerve is at least partly responsible for its susceptibility to causalgia following injury.

AETIOLOGY.—The vasodilatation which is so prominent a feature of causalgia has led to the almost inescapable conclusion that the condition, if not predominantly, is at least partly a vasomotor phenomenon. A similar redness and heat can be produced in the corresponding skin territory of a cutaneous nerve when it, or a posterior nerve root, is cut and the distal end stimulated electrically. The explanation of this fact is not easy. It has never been clearly shown whether or not "anti-dromic" (proximo-distal) impulses are being conveyed along sensory nerve fibres, whether it is due to stimulation of efferent nerves which accompany sensory nerves and have their cell stations in the posterior root ganglia or to excitation of a, as yet unfound, "nocifensor" peripheral nerve plexus.[11] Since the signs and symptoms of causalgia are seldom strictly confined to the anatomical territory of the affected nerve there seems to be little doubt that the effects are mediated by the release of vasodilator substances which spread over a considerable area from the stimulated end organs. The pain can be explained on the same grounds as the vasodilatation since peripheral pain can be produced by distal stimulation of a cut peripheral nerve. The predominant importance of dorsal root participation in causalgia is supported clinically by the herpetic lesions of the skin which may complicate causalgia since it is well known that herpes zoster, in which the skin lesions may take a form indistinguishable from causalgia, is frequently associated with lesions of the posterior root ganglia.

The most plausible explanation appears to be that chronic irritation of a peripheral nerve stimulates nerve fibres of the posterior root system. A distal reaction results whereby irritating substances are released into the skin and produce therein vasodilatation. It is from this area of skin, rather than from the nerve at the site of injury, that pain impulses arise to be carried back along the same or adjoining nerves to the sensorium. This explanation is substantiated by the observation that division of the involved nerve distal to the point of injury or irritation results in complete relief of symptoms. Unfortunately in some severe cases the failure of all methods of treatment, including spino-thalamic tractotomy, suggest that there may be a central or psychic sensitisation to pain as well as the purely local phenomena described above.

CLINICAL FEATURES.—The symptoms of causalgia may be out of all proportion to the severity of the original injury and, along with the patient's mental anxiety and fear of pain, may lead to a diagnosis of malingering or psychoneurosis being made. There is no doubt that a large psychological

overlay may be responsible for the maintenance of symptoms particularly when pension or compensation claims complicate the injury.

The outstanding symptom is intense, burning pain in the distal territory of the involved nerve which, being most commonly the median, is the outer aspects of the hand. The pain is first noticed within a few days or weeks of the original injury which might have been only trivial. Not infrequent following war wounds the same symptoms may develop in amputation stumps,



FIG. 322
Causalgia arose in the left hand which shows all the features of median nerve injury.

lacerations of the digits or even following "sprains" where it would seem to be an exaggerated form of Sudeck's atrophy. This resemblance has led one author to call the latter condition "minor causalgia"[9] The burning pain increases in intensity as time goes on until it is exquisite and accompanied by a like degree of tenderness in the corresponding area. The tenderness is superficial and with the pain is exaggerated by the slightest contact or distortion of the part The slightest pressure, sudden movements or changes in temperature, particularly exposure to warmth, provoke such severe exacerbations of burning pain that the patient cringes from the slightest threat of contact. Holding the limb flexed and guarded by the healthy member the patient may at times carry the hand wrapped in cold, wet bandages to obtain relief. The pain differs from that of neuritis in that it spreads beyond the anatomical limits of the affected nerve and is characteristically accompanied by definite objective phenomena In some patients causalgia affects adjacent digits as well as the one injured.

When the affected limb is examined

warmer than its fellow (Fig. 322). The skin is usually wet with sweat and exquisitely hyperaesthetic. The slightest distortion of the part will set off recurring waves of pain which persist long after the stimulus has ceased. Occasionally a few blisters will be noted and sometimes a distinct herpetic eruption is encountered. At a later stage the skin becomes dry, scaly and cold and the pain may now be less intense. Finally all the signs of disuse atrophy develop and X-rays of the bones will demonstrate diffuse decalcification. The patient may become so nervous and mentally upset with anticipation of pain that he is on the verge of mental breakdown. Psychoneurosis, drug addiction and attempts at suicide have been reported.

TREATMENT.—It is wise to persist with conservative measures for so long as the patient can be encouraged in them. The pain, intractable at first, may continue for a year or longer but after a year the condition tends to subside and in the majority of instances will have disappeared completely within a few years. Occasionally the favourable settlement of a pension or compensation claim is attended by considerable improvement.

The patient soon learns to keep the affected part cool and protected from contact and extremes of temperature so that much pain can be avoided. The condition of the skin is usually resistant to all forms of local treatment. If the symptoms continue for longer than the patient can bear, something must be done to afford him relief. Tinel's operation of dividing the nerve distal to the site of irritation gives certain relief but in the case of the median nerve is followed by serious paralysis and anaesthesia. Neurolysis, with or without excision of the scarred segment of nerve and resuture, is the procedure of choice but is not infrequently followed by a recurrence of pain. When causalgia complicates an amputation stump excision of a neuroma, if present, or reamputation may be attempted but almost invariably the latter is followed by further reamputations at higher levels. Because there is a prominent vasomotor component to causalgia interruption of the sympathetic pathways would seem to be a procedure of some value. This is the case if patients are carefully selected beforehand. The best method of selection is to perform a paravertebral block and should the symptoms be relieved for at least two hours a sympathectomy may be performed with reasonable hope of permanently relieving the symptoms. On occasion cure has followed the paravertebral block alone. On no account should an operation be performed without a prior evaluation of the mental state of the patient since no surgical measure will be effective when there is a strong psychogenic background or if litigation or compensation claims are outstanding.

In rare cases spino-thalamic tractotomy and even such measures as intracranial tractotomy and prefrontal leucotomy have been performed but such radical procedures must be considered only in desperate cases. It is best not to begin climbing the nervous tree for once the climb is started relief is seldom attained until, or even when, the tree is "topped." The success of medical measures is attested by the fact that the causalgias of the Second

World War have nearly all now subsided. Thus it is best to persist with conservative measures and only operate when these fail after prolonged trial.

ERYTHRALGIA; ERYTHROMELALGIA

The terms erythralgia,[11, 12, 13] erythromelalgia[16, 5] and erythermalgia[17] have all been applied to a syndrome in which there is redness, a peculiar form of burning pain or tenderness of the extremities, most frequently the lower, and, in all cases of primary erythralgia and most of secondary erythralgia, associated heat of the affected limb. A great deal of confusion as to exact nomenclature can be avoided by accepting the syndrome as an entity of which there are two clinical types: **primary** or **idiopathic** erythralgia which occurs in the absence of any detectable organic disease of the nervous or vascular systems and **secondary** erythralgia which is an expression or an accompaniment of some underlying local or general disease, not infrequently obliterative vascular disease. The primary form is quite rare and most vascular clinics may count themselves fortunate to see a true case every two or three years. When encountered and when no cause can be found after most careful study it must be considered as a clinical entity even though some authorities disagree. The secondary form is not uncommon being most frequently encountered in association with atherosclerosis and thromboangiitis obliterans of the peripheral blood vessels especially when sepsis or ulceration is present. Patients who have chronic chilblains often suffer from erythralgia in the summer months. It has been described as an aftermath of immersion foot and frostbite and when ulceration complicates the post-phlebitic state erythralgia is frequent. We have encountered an "erythralgic-like" state following lumbar sympathectomy[14] and such general diseases as hypertension, diabetes and polycythemia rubra vera have had erythralgia as an accompanying complication.[3]

The etiology of the idiopathic form is not known and all that [illegible] of the second [illegible] and [illegible] of [illegible] has been little or no opportunity of examining limbs the seat of the primary form and those with the secondary form show only the pathology of the associated disease. The [illegible] of the primary form [illegible] is not an entity. I[illegible] is in fact the precur[illegible] latent disease much as migratory phlebitis may be a very advanced herald of thromboangiitis obliterans.

PROBABLE MECHANISM OF ERYTHRALGIA.—The three clinical features of erythralgia, namely redness, *heat* and pain, are the main features of inflammation. Inflammation is a *non-specific* response of tissues to an irritant which may be physical, chemical or bacterial. Likewise erythralgia is an inflammatory-like response of tissues to an irritant, known or unknown, which may be acting locally or from a distance. In many cases a local inflammatory

warmer than its fellow (Fig. 322). The skin is usually wet with sweat and exquisitely hyperaesthetic. The slightest distortion of the part will set off recurring waves of pain which persist long after the stimulus has ceased. Occasionally a few blisters will be noted and sometimes a distinct herpetic eruption is encountered. At a later stage the skin becomes dry, scaly and cold and the pain may now be less intense. Finally all the signs of disuse atrophy develop and X-rays of the bones will demonstrate diffuse decalcification. The patient may become so nervous and mentally upset with anticipation of pain that he is on the verge of mental breakdown. Psychoneurosis, drug addiction and attempts at suicide have been reported.

TREATMENT.—It is wise to persist with conservative measures for so long as the patient can be encouraged in them. The pain, intractable at first, may continue for a year or longer but after a year the condition tends to subside and in the majority of instances will have disappeared completely within a few years. Occasionally the favourable settlement of a pension or compensation claim is attended by considerable improvement.

The patient soon learns to keep the affected part cool and protected from contact and extremes of temperature so that much pain can be avoided. The condition of the skin is usually resistant to all forms of local treatment. If the symptoms continue for longer than the patient can bear, something must be done to afford him relief. Tinel's operation of dividing the nerve distal to the site of irritation gives certain relief but in the case of the median nerve is followed by serious paralysis and anaesthesia. Neurolysis, with or without excision of the scarred segment of nerve and resuture, is the procedure of choice but is not infrequently followed by a recurrence of pain. When causalgia complicates an amputation stump excision of a neuroma, if present, or reamputation may be attempted but almost invariably the latter is followed by further reamputations at higher levels. Because there is a prominent vasomotor component to causalgia interruption of the sympathetic pathways would seem to be a procedure of some value. This is the case if patients are carefully selected beforehand. The best method of selection is to perform a paravertebral block and should the symptoms be relieved for at least two hours a sympathectomy may be performed with reasonable hope of permanently relieving the symptoms. On occasion cure has followed the paravertebral block alone. On no account should an operation be performed without a prior evaluation of the mental state of the patient since no surgical measure will be effective when there is a strong psychogenic background or if litigation or compensation claims are outstanding.

In rare cases spino-thalamic tractotomy and even such measures as intracranial tractotomy and prefrontal leucotomy have been performed but such radical procedures must be considered only in desperate cases It is best not to begin climbing the nervous tree for once the climb is started relief is seldom attained until, or even when, the tree is "topped." The success of medical measures is attested by the fact that the causalgias of the Second

by the time the patient presents for advice, aggravation of the distress by exposure to warmth, in bed at night, by walking or other forms of stimulation will have been appreciated by the sufferer and are likely to be spontaneously mentioned. The discomfort is alleviated by exposure to cold and by elevation of the limb, measures which relieve the tension and reduce the blood flow. The patient may have learned these facts and will state that relief has been obtained by such measures as sleeping with the limbs exposed, walking about on the cold floor or immersing the limbs in cold water or wrapping them with cold, wet towels



FIG. 323
Ruboric limbs—the seat of obliterative arterial disease and severe secondary erythralgia.

During an attack the skin is bright red and tender to the slightest touch, much like a first degree burn. The skin is *warm or hot*, particularly in the idiopathic form of erythralgia and in *those secondary* forms associated with sepsis or ulceration. *In secondary* erythralgia secondary to obliterative vascular disease, in the absence *of infection*, the skin may be red, very tender to the touch but cold even though *the* patient complains bitterly of a burning or throbbing pain and *subjective* heat (Fig 323) The red ... of the ...

... absence of arterial disease the peripheral pulses

process is demonstrable as in obliterative vascular diseases, chronic chilblains or the post-phlebitic state. But in some cases no local process can be found and here it must be postulated that some unknown, but normally subliminal stimulus is provoking an inflammatory response in a susceptible individual The ultimate mechanism is considered to be neuro-chemical in that some unknown chemical substance, perhaps akin to histamine, is released into the tissues from irritated cells and acts by lowering the threshold of the pain nerve endings to various forms of stimulation[11, 13] which may be apparent in the secondary form but quite unknown, at the time at least, in the idiopathic form. The release of these substances, as in inflammation, dilates local blood vessels so that heat and redness ensue as well as the characteristic unnatural tenderness of the skin. The pain nerve endings in the skin seem to be particularly susceptible to minor alterations in heat and tension. The critical temperature at which distress can be produced varies from patient to patient but commonly lies within the range of 32° to 36°C. In practice placing the feet in warm water, as when having a bath, produces extreme distress as may also the vasodilatation produced by sleep. The patients may sleep with their feet outside the bed in order to reduce or maintain the temperature below the " critical point " of discomfort. Alterations in the tension of the skin, as by the spontaneous engorgement of dependency, or the artificial engorgement which follows inflation of a blood pressure cuff often induces an attack. In such instances there is a subjective feeling of heat which may not always be accompanied by objective heat, just as in some instances of secondary erythralgia in obliterative vascular diseases. However, this does not justify the use of yet another term, *e g.* erythermalgia, as suggested by some authors.[19] Friction, too, is a common aggravating agent and when combined, as in walking, with vasodilatation and engorgement of the limbs, may precipitate pain so intractable that the patient becomes a cripple. In short, the skin of an erythralgic extremity is in a state of unnatural sensitivity to degrees of warmth, tension and friction which in the normal individual would be insufficient to stimulate the pain nerve endings but which in this condition lead to the development of a clinical state characterised by redness, burning pain and, in most cases, heat. An example of all these features is the erythralgic state which exists in an acute sunburn, a condition with which most people are familiar and which is made manifestly worse by heat, friction and increased tension.

Clinical features.—Erythralgia may affect either sex. The idiopathic form is more likely to occur in young adults while the secondary form usually develops from middle age on but the age of onset depends largely upon the associated disease. Although any part of the body may be affected, including the accessible mucous membranes, it is the lower extremities which most often suffer. Both limbs are involved in most cases but one limb only or a small part of a foot for example may alone be involved. At first the attacks may occur only in the warm weather but later they appear at all seasons and.

regulatory sweat secretion, which is predominantly operative through the sweat glands of the trunk, there is a nervous type of sweating in response to psychic influences, i e fear, nervousness, pain, fatigue and mental effort. This is a normal response of the body to states of tension and, in contrast to the thermoregulatory type of perspiration, the sweating occurs most noticeably on the forehead, the palms of the hands and the soles of the feet. In some individuals, for reasons unknown, there is periodic excessive sweating in these regions in response to psychic stimuli which in the normal individual would elicit no alteration in sweat production. It is most probable that such hyperidrosis is the result of overaction of the sympathetic nervous system to stimuli from the higher centres, *i.e.* hypothalamus and cerebrum. In this respect it is merely an exaggerated pattern of the "cold sweat" which accompanies alarm reactions in the normal person

The excessive sweating which is the result of central nervous system overaction is known as **primary or essential hyperidrosis**.[illegible] As well as this there is secondary hyperidrosis which is a symptom of a local or general disease In either case interruption of the sympathetic nerve supply to the affected part abolishes the sweating response The sweat glands are not [illegible]

be rer [illegible]

with [illegible] nerve trunks and ganglia along with the adrenergic pathways to the blood vessels, *the* sweat glands themselves are cholinergic. In other words sweat glands are anatomically sympathetic but pharmacologically parasympathetic.

AETIOLOGY — Primary or essential hyperidrosis is so named because no aetiological agent can be demonstrated The condition is of cortical and hypothalamic origin and manifests itself by [illegible]

[illegible] In some instances there is a [illegible] tendency and the condition *has been* said to be more common in those of an unstable emotional make-up It has been suggested that essential hyperidrosis is the translation of a mental or emotional conflict *into* a physical defect—*in* short a psychosomatic disease It is more probable that a neurotic tendency, if present, is the result, not the cause, of the sweating since the social problems accompanying severe hyperidrosis make the most stable of its victims at least introspective. In some individuals an anxiety state develops which in itself *tends* to perpetuate the sweating and a hyperidrosis initially periodic, may become virtually continuous during the waking hours.

None of the patients with essential *hyperidrosis* sweat whilst asleep and most are free from attacks whilst they are alone and undisturbed or when in the presence of those they know When they encounter strangers or become

are normally palpable or bounding during an attack. The pain is increased by pinching or stroking the skin and by the application of warmth. Relief is obtained by the application of moderate cold and by elevation. Extremes of cold, as by the application of ice, induce pain indistinguishable from that induced by heat. In severe cases the fear of pain may reduce the patient to invalidism and affect the mental state.

Special examinations during an attack may reveal the skin temperature to be elevated from 5° to 15° above that of the normal limb in the same environment. Arterial pulsations have been demonstrated to be of greater amplitude by the oscillometer and an elevated oxygen content in the venous blood flow from the affected limb has been described.[3, 19] Such findings have been advanced as support for the vasomotor basis of the syndrome, but they are only such as would be expected in any limb the seat of increased blood flow and are by no means universally found in erythralgia. Generally speaking no special tests are necessary to make the diagnosis since the clinical features of erythralgia are so distinctly characteristic.

TREATMENT.—When an underlying cause for the condition can be found, that disease must be treated, and with its control the symptoms of erythralgia are usually relieved. When no underlying disease can be found general measures alone must be adopted in the first instance. It is best to avoid opiates because of the danger of drug addiction It is a fact that considerable relief may be obtained from the use of acetylsalicylic acid, grains v. Bed rest and emergency measures such as exposure of the feet to cold air, immersion in cool water or wrapping with wet towels may be resorted to. Local measures are poorly tolerated but if continuously and carefully applied an increasing tolerance for graded physiotherapy such as diathermy and massage may be developed with benefit. Lumbar sympathectomy may completely relieve the symptoms as well as improve the local circulation if the condition is secondary to vascular insufficiency. It should not be done in other cases unless an attack can be terminated by paravertebral block and, whilst the block continues, further attacks cannot be precipated by those artificial means which in the absence of block produce an attack.

HYPERIDROSIS

The only derangement of sweating which may be so disabling to the sufferer that medical advice is sought is that of excessive sweating of a non-thermoregulatory type. The commonest stimulus to sweat secretion is a rise in the temperature of the circulating blood, the most frequent causes of which are an increased environmental temperature, exercise and fever. Sweating results from the direct action of the warmed blood on the heat centres, chiefly in the hypothalamus, and by a reflex induced by stimulation of heat receptors in the skin. Thus body sweating helps to eliminate heat and to maintain the body temperature within normal limits. Apart from this purely thermo-

Sweat glands are most numerous on the hands, the feet and the face and in primary hyperidrosis all these glands are overactive to a greater or lesser degree whereas in secondary hyperidrosis the sweating is limited to that part of the body stimulated, usually an extremity. With this exception and those of localised paroxysmal hyperidrosis and gustatory sweating the features of essential hyperidrosis are so characteristic that diagnosis is never a problem.

The main clinical features are intermittent and remittent bouts of excessive sweating of a symmetrical nature and " emotional " or " mental " distribution that is involving the hands, feet and, usually to a lesser extent, the face. The limbs are dry upon awakening but the skin soon becomes excessively moist and bursts of excessive sweating in which the hands and feet literally " drip " are fired off by excitement, fear, embarrassment or mental concentration. Most patients have suffered for many years or " as long as I can remember." At first the symptoms may have been mild only to become a burden or socially intolerable when stress has become severe as in adolescence, business competition, drafting into the army or entry into a profession. This helps to explain why the average age at which advice is sought is about twenty-three years. By this time the sweating may have been socially and economically intolerable and there may be no remissions during waking hours. If the sweat is malodorous an additional burden is placed upon the patient who may be completely shunned by others. The economic burden of replacing rapidly rotting stockings and footwear alone may force the patient to seek a cure for the condition. Cases have been reported in which thirty-six pairs of shoes were needed yearly, and in which the boots have had to be emptied of water several times a day. If the patient is a surgeon perspiration may overflow from his rubber gloves.[23] It is little wonder that psychological stress is frequently present since the patient retreats more and more from social contacts and extreme introversion or anxiety states, perpetuating the hyperidrosis, may develop.

A family history may be elicited but we have never obtained any. Although a male predominance has been reported a closer study of cases reported in the literature shows an almost equal incidence between the two sexes; this has also been our personal experience. Once established, essential hyperidrosis always progresses. A spontaneous cure has not been reported in the literature to date but we have had one young woman whose parents refused operation at the age of fifteen years improve so much that at the age of nineteen years surgery was no longer considered necessary.

Examination of the limbs reveals nothing except the excessive sweating and during the examination sweat drips from the finger tips or gathers in a puddle in the palm of the cupped hand (Fig 324). The hands may feel cool and be slightly cyanotic as a result of the heat loss from evaporation but the superficial veins show no abnormality and all of the arteries pulsate normally. Inter-digital fungus infection is common especially in the feet which, having less opportunity to dry, may become tender, macerated and

emotionally or mentally stimulated sweat begins to drip from their hands and feet. In most instances the face and all four limbs are affected, the hands being the most troublesome. Rarely hyperidrosis may be localised to a part of a limb or the face. Localised paroxysmal hyperidrosis in a limb has been reported not infrequently[16] and we have seen it in a boy on the ulnar aspect of the forearm near the wrist. As with the generalised form no cause can be demonstrated. A localised reflex sweating may occur on the face in response to eating spicy foods, in fact just such a response may develop in most people if curry is hot enough! Known as **gustatory sweating,** it occurs rarely after suppuration and open wounds of the parotid gland, parotidectomy and cervico-dorsal sympathectomy.[7, 8] It has occurred only once in our series of nineteen cervico-dorsal sympathectomies for hyperidrosis. Its mechanism is obscure, though it may be due to some substance, possibly acetylcholine, released by the secretory nerve of the parotid gland, and acting on nearby sweat glands, or it may be the result of cholinergic fibres growing distally into the divided end of the auriculo-temporal nerve. Why it should follow sympathectomy is unknown. Similarly the causes of localised and generalised essential hyperidrosis are quite unknown. No detectable abnormality has ever been noted in the sweat glands, sympathetic ganglia or chains so that a local anatomical fault can be excluded. Until more concrete data are at hand it must be concluded that essential or primary hyperidrosis is a peripheral manifestation, through the sudomotor component of the sympathetic nervous system, of an exaggerated cortical and hypothalamic reaction to every day situations which normally would have no effect on the sweating mechanism.

Secondary hyperidrosis is more a symptom of a local or general disease than a syndrome or disease in its own right. Whereas primary hyperidrosis is a functional disease arising from stimulation from higher centres, the secondary form occurs when the stimulus arises from levels below the brain and an organic cause usually can be found The neurovascular conditions which may be complicated by hyperidrosis include traumatic, irritative and inflammatory lesions of the spinal cord such as poliomyelitis and syringomyelia, causalgic states of the peripheral nerves, Sudeck's atrophy, cervical rib, and the late stages of frostbite and immersion foot In most of these there is a history of trauma, a partial injury to a nerve or inflammation or irritation of the peripheral part of the somatic or sympathetic nervous or vascular system of the limb. A frequent association is hyperidrosis in the foot of a limb the seat of a gravitational ulcer. The excessive sweating tends to perpetuate the ulcer and it is in situations such as this that sympathectomy is beneficial. Similar unilateral or localised sweating may accompany other local inflammatory conditions of the extremities and also may be present in association with a glomus tumour.

CLINICAL FEATURES —*Apart from the ability to find a precipitating or at least an associated factor in secondary hyperidrosis the only real difference between essential and secondary hyperidrosis is the extent of involvement.*

advantage that both sides may be done at the one sitting. For the lower limb lumbar sympathectomy with the removal of the second and third lumbar ganglia and the intervening chain will give permanent relief. Recurrence has not been reported, nor has it followed sympathectomy in our experience. Some degree of moistness does return with the establishment of alternative sympathetic pathways particularly in the upper limb but the degree of moistness is

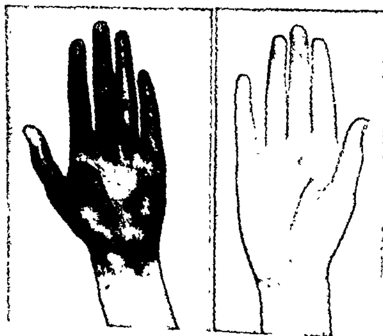


Fig 325
Starch test to show abolition of sweating after right cervico-dorsal sympathectomy.

never troublesome and is, indeed, welcome since many sympathectomised patients complain of the excessive dryness of their hands in particular. When excessively dry the use of pure lanolin rubbed into the hands will make them more comfortable. When all four limbs have been [illegible] body sweating may be complained of. [illegible] ate region but may be a serious source [illegible] Generally speaking an individual who [illegible] quadrilateral sympathectomy seldom complains of excessive sweating on his trunk unless the environmental temperature and humidity is high or unless activities are pursued which stimulate thermoregulatory mechanisms. [illegible]

[illegible] guaranteed by sympathetic [illegible] deal, for an unequivocal denervation of the affected limb.

R. B. L.

malodorous. Local infections are common and heal slowly. If the sweating is secondary to a focus of local infection such as a stasis ulcer the causative inflammation is aggravated by the excessive moisture.

TREATMENT.—Conservative measures such as 5 per cent. formalin, foot and hand baths may be tried and although they may control some of the milder cases there is considerable risk of a dermatitis developing. Alum



FIG. 324
Hyperidrosis in an eighteen year old nurse, showing the maceration and fungus infection which frequently complicates the condition.

solutions are seldom effective and superficial X-ray therapy to abolish sweat gland activity must be pushed to a level at which radiation dermatitis and skin necrosis are real dangers. On the whole, measures designed to damage the sweat glands do not cure, rarely alleviate and run the risk of damaging the skin.

Recently several encouraging reports have followed the administration of anticholinergic drugs taken by mouth. The most successful of these drugs have been banthine and hydergine given alone or in combination[4, 6] Fifty to 100 mg. of banthine given four hourly is recommended for relief of symptoms; in this dosage it produces few side reactions Even so dilatation of the pupils sufficient to make reading troublesome or impossible, dryness of the mouth and constipation may be real complaints. The drugs must be taken continually and since none of them is purely anticholinergic and all have multiple effects they are still on trial.

The only manner in which permanent relief can be guaranteed is by sympathetic denervation of the affected part[1, 7, 8, 22] (Fig. 325) This was first performed for hyperidrosis in 1919. For the upper limb the Telford type of cervico-dorsal sympathectomy is completely satisfactory and possesses the

advantage that both sides may be done at the one sitting. For the lower limb lumbar sympathectomy with the removal of the second and third lumbar ganglia and the intervening chain will give permanent relief. Recurrence has not been reported, nor has it followed sympathectomy in our experience. Some degree of moistness does return with the establishment of alternative sympathetic pathways particularly in the upper limb but the degree of moistness is

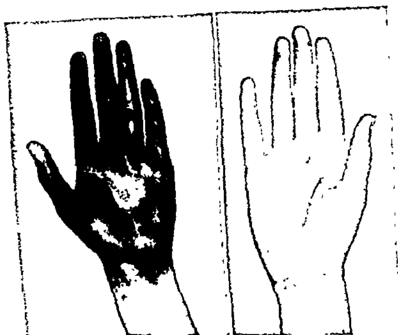


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never troublesome and is, indeed, welcome since many sympathectomised patients complain of the excessive dryness of their hands in particular. When excessively dry the use of pure lanolin rubbed into the hands will make them more comfortable. When all four limbs have been denervated, compensatory body sweating may be complained of. This is seldom troublesome in a temperate region but may be a serious source of discomfort in a hot, humid climate. Generally speaking an individual who has had a quadrilateral sympathectomy seldom complains of excessive sweating on his trunk unless the environmental temperature and humidity is high or unless activities are pursued which stimulate thermoregulatory mechanisms. In either case they learn to avoid such conditions as exaggerate thermoregularity sweating and the sufferer from hyperidrosis is as satisfied a patient as a surgeon can treat, for an unequivocal cure can be guaranteed by sympathetic denervation of the affected limb.

R. B. L.

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CHAPTER XVIII

THE VASCULAR EFFECTS OF SUPERIOR THORACIC OUTLET SYNDROMES

(Particularly those associated with Cervical Rib[1, 2])

FIVE or six per cent of patients suffering from neuritic manifestations of cervical rib present vascular disturbances in the upper extremity, and more than forty cases have been recorded of vascular anomalies unaccompanied by brachial neuritis. Similar symptoms have been recorded in the absence of a cervical rib, when it may be that some constricting band of fascia, or a hypertrophied or prominent scalene muscle causes an interference with the neuro-vascular bundle with symptoms resembling those usually attributed to cervical rib

The vascular disturbances fall into two groups, local in the shoulder and distal in the hand.

In the shoulder there may be prominence and excessive pulsation of the subclavian artery and rarely[3] there may be a bruit or a thrill Only exceptionally (*see* below) does actual aneurysmal dilatation occur.

Distally, the radial pulse may be lessened in amplitude or obliterated in certain positions of the shoulder joint. It may disappear in the position of attention when the shoulder is braced downward,[4] or when it is braced backward,[3] or adducted against resistance,[5] or abducted,[6] or abducted and extended backward,[7] or rarely when the neck is hyperextended.[8] The hand may be subject to pallor, cyanosis, paraesthesiae, cramping pain, Raynaud's phenomenon, acrocyanosis, finger-tip necrosis, or even digital gangrene. Occasionally the arm veins are obstructed too. These effects on the circulation are almost exclusively unilateral Once vascular symptoms appear they tend to be progressive A summary of reported cases and a full guide to the literature will be found in Eden's paper.[9]

The cause of the vascular symptoms of cervical rib is disputed and as Telford and Mottershead[3] have [illegible] of 120 of their own patients, [illegible] some in one case and some in [illegible] obliterating the radial pulse, make it rather unlikely that the obliteration can [illegible]

[illegible] that simple [illegible] of the subclavian artery by bone or other structure is not always responsible is clear from the observation that sometimes when the radial pulse is obliterated an axillary pulse is palpable below the level of the clavicle?

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The cause of the vascular symptoms of cervical rib is disputed and, as Telford and Mottershead[5] have convincingly argued from a close study of 120 of their own patients, the diversity of movements which are effective, some in one case and some in another, in obliterating the radial pulse, make it rather unlikely that the obliteration can [illegible]

[illegible] That simple [illegible] of the subclavian artery by bone or other structure is not always responsible is clear from the observation that sometimes when the radial pulse is obliterated an axillary pulse is palpable below the level of the clavicle[7]

Murphy[10] believed that the subclavian artery was compressed between the cervical rib and scalenus anterior, but this explanation is not applicable to cases in which the vascular symptoms persist, as they frequently do, after scalenotomy. It is frequently possible to demonstrate at operation that if the pulsation at the wrist is abolished by a suitable manoeuvre, it more often than not can still be felt in the arterial trunk beyond the outer border of scalenus anterior. This explanation would also run counter to the general rule that a healthy artery stretched over bone erodes the bone but is not compressed by it; where several hypotheses are in competition, one which appears to be a unique exception to the manner in which tissues usually behave can generally be discarded.

Todd[11, 12, 13] advanced the view that the vascular symptoms in the hand were due not to arterial compression but to paralysis of the sympathetic nerves in the lowest trunk of the brachial plexus, whose relation to the cervical rib is much more intimate that that of the artery. Leriche[14] showed, however, that the vascular symptoms were those of irritation rather than paralysis of sympathetic nerves, and suggested that the mechanism might be one of compression-irritation of the peri-arterial plexus of the subclavian artery; since the distribution of this plexus has subsequently been shown to be local over a short segment of the arterial trunk, such a mechanism cannot be applied to distal vascular changes in the hand. Telford and Stopford[15] returned, however, to Todd's hypothesis and postulated a sympathetic irritation of the sympathetic component of the lowest trunk. Blair, Davies and McKissock[16] supported this theory, but reported that at autopsy the sympathetic fibres were not grouped together in a single bundle on the under surface of the lowest trunk, where they might have been subjected to selective compression, but were scattered through it in such a pattern as to be anatomically no more vulnerable than the other constituent fibres of the same trunk. The strongest argument against the theory of sympathetic irritation is that sympathetic nerves are notoriously difficult to maintain in a state of long-continued irritation; irritation is quickly superseded by paralysis; yet signs of sympathetic paralysis, a dry, hot, red hand with dilated veins, are seldom seen in association with cervical rib. Moreover, the vascular cases are distinct from the nervous, as they would not be if due to a common nervous cause.[16]

Lewis and Pickering[17] rejected the nerve-compression theory as an explanation of the vascular symptoms of cervical rib, and suggested rather that trauma to the vessel wall led to mural thrombosis and the liberation of multiple emboli. This theory, too, is vulnerable. The vascular symptoms can often be varied in degree by alterations in the position of the arm; were they always due to embolic occlusion the vascular episodes would be less transient than they sometimes are, and less susceptible of relief by changes in position. Yet the embolic hypothesis, better than any other, fits the almost invariably unilateral incidence of the vascular effects. Telford and Mottershead found thrombotic change in fourteen of their 120 cases. In twelve of these the upper

limit of the thrombosis lay no higher than some point between the bifurcation of the brachial artery and the lower border of pectoralis major. In the remaining two cases the thrombosis extended higher but did not even in these reach the cervical rib.

Eden[7] subscribed to the thrombo-embolic theory of Lewis and Pickering, but decided that the cause of arterial trauma was not musculo-osseous compression in the angle between scalenus anterior and rib but "costo-clavicular compression" between the clavicle and a cervical rib, or the clavicle and an abnormal first rib. This compression, he claimed, produced dilatation and mural thrombosis in the subclavian artery as it lies in the canal between neck and axilla; from the subclavian thrombi emboli are detached to lodge in digital vessels with a resulting Raynaud's phenomenon, or in a larger vessel with progressive thrombosis spreading from the impacted embolus to affect a considerable segment of the main arterial trunk, not necessarily extending *upwards to* the point of compression [illegible] ogressively after removal of the cervical rib or [illegible] *Whether* the subclavian artery *can* be comp[illegible], and if so, what *position of the* shoulder is most likely to narrow the costo-clavicular space, *continues to be* argued Stammers considers that the level is important to which the arch *of the subclavian* artery rises in the neck.

Telford and Mottershead[3] are in a strong position in claiming that the symptoms of cervical rib *cannot all be* ascribed to a single cause. They divide cases into two *main groups. In* one of these, the smaller, they consider costo-clavicular *compression, in abduction and bracing of the* shoulder, to be responsible for symptoms referable *to the whole* plexus. More commonly, they find that downward *extension of the* arm at the position [illegible] produces [illegible] a cervi[illegible] has an [illegible] rib, or between the converging heads [illegible] the median nerve. [illegible] when that occurs, th[illegible] to compression of t[illegible] heads of *the median* nerve.

When Raynaud's *phenomenon* occurs in association with cervical rib, it by no means necessarily *follows that* this is the result of the anomalous rib[12, 13]. A female *patient* who presents with *Raynaud's* phenomenon in the fingers of both hands, unaccompanied by signs of brachial plexus irritation, should be regarded as suffering from "Raynaud's disease," *or scleroderma*, even if she has a cervical rib; the vascular *symptoms of cervical* rib are unilateral in 98 per cent of cases, and in the 2 per cent. of bilateral cases they are asymmetrical and the responsibility of the *rib* is doubtful *or partial*. It is of interest in this connection that of patients presenting *with purely* nervous symptoms referable to cervical rib, less than 10 per cent. are male. Important in the diagnosis of the vascular symptoms of cervical rib is *syringomyelia*. This

disease may first attract the patient's attention by colour change and other vascular disturbances, often of Raynaud's type, in the hand.

Aneurysmal dilatation of the subclavian artery in association with cervical rib was first described by Murphy,[11] and of the reported cases of vascular anomalies with cervical rib subsequently published approximately one-third have presented at operation a fusiform dilatation or substantial aneurysm of the third part of the subclavian and sometimes of the axillary artery as well. It was remarkable to Murphy, and it still is remarkable, that the dilatation is invariably distal to the point of apparent "compression" of the vessel. Halsted,[24] inspired to an experimental investigation by this phenomenon, succeeded in producing aneurysmal dilatation of the aorta of dogs distal to aluminium bands applied to produce incomplete stenosis. If simple narrowing of the lumen were the cause of the distal dilatation one would expect the lumen of the aorta to be dilated beyond a coarctation, yet the aorta beyond a coarctation is contracted, though its branches are enlarged Perhaps *the metallic bands exert some other effect than simple compression.* It may indeed be that in these experiments, and in subclavian aneurysm complicating cervical rib in man, the dilatation of the artery distal to the point of compression is due to paralysis of the sympathetic plexus in the adventitia; the limited distribution of the aneurysm corresponds roughly to that of the plexus.

One of us (I. A.) had the privilege of assisting Mr J. M. Graham in his management of a middle-aged lady who suffered from bilateral cervical rib with bilateral fusiform aneurysm of the subclavian and axillary vessels; on each side the aneurysm extended distally from the lateral border of the rib The Wassermann reaction was negative. Both cervical ribs were excised and both subclavian arteries were ligated in their first parts. All symptoms were relieved *The case seemed an important one,* and was prepared for publication. The late D. M. Greig, consulted about the conclusion to be drawn from Graham's observations regarded in the light of Halsted's work, refused to credit that a *healthy artery could be compressed by bone. The patient* subsequently, and in spite of a negative Wassermann reaction, developed a gumma of the leg The principle cited by Greig, and subsequently supported by the event, may have a wider application than to that single case.

Eden[9] believed that associated subclavian aneurysm, occurring as it does distal to the cervical rib, is due to costo-clavicular compression and that the dilatation occurs at the point compressed.

I. A.

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CHAPTER XIX

THE COAGULATION OF THE BLOOD

COAGULANTS AND ANTICOAGULANTS

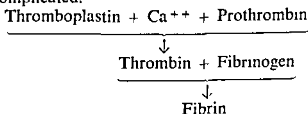
THE normal clotting mechanism becomes of increasing complexity with advancing knowledge, and is still far from being fully understood The last stage of the process, that of fibrin formation, is the only one which can be observed, and the changes in the blood leading up to this final reaction can only be inferred. " The blood contains within itself not only the clotting factors that will initiate, accelerate and limit coagulation as required, but also a series of safety devices to prevent coagulation occurring within the vessels and for dissolving fibrin which is no longer useful.[1]" The subject has recently been reviewed by Biggs and Macfarlane[1] and Quick[2] and modern knowledge of the process has advanced from their observations and their correlation of many experimental data.

A fibrin clot forms as the result of interaction between thrombin and fibrinogen. Fibrinogen is normally present in the blood stream, but thrombin has an enzyme-like action and a minute quantity is sufficient to cause coagulation of all the blood in the body. The formation of thrombin is, therefore, the key to the process of clotting.

Thrombin is a protein complex derived from the interaction of prothrombin, ionisable calcium and thromboplastin (thrombokinase). The first two substances are normally present in the blood stream, and it is therefore on the formation of thromboplastin that coagulation of the blood finally depends

Thromboplastin in normal clotting is formed by a series of reactions involving anti-haemophilic globulin, Christmas factor, factors V and VII, calcium ions and a material present in platelets. A substance with similar properties, tissue thromboplastin, is derived from damaged tissue cells and is responsible for clotting in abnormal circumstances.

The basic process can be represented graphically, although it is in fact vastly more complicated.



The influence of these various factors, and the conditions in which they are deficient, may be considered shortly.

Fibrinogen.—Fibrinogen is a globulin, synthesised in the liver. Clinical deficiency or absence of fibrinogen is rare, and when it occurs may be either a primary deficiency, or secondary to other disease. In primary deficiency there is an inborn error of its formation, and consanguinity amongst parents or grandparents has been frequently observed in such cases[3] The clinical symptoms are similar to but less severe than those of haemophilia and only two deaths have been reported out of eleven cases recorded A normal blood transfusion will usually supply a sufficient amount of fibrinogen to last for several days.[4] Secondary fibrinogen deficiency occurs in certain cases of malignant disease and infections of the bone marrow, in acute liver atrophy and rarely in association with toxaemia of pregnancy, when in some cases the blood has been rendered incoagulable.[5]

Prothrombin.—Prothrombin is formed in the liver, for which purpose vitamin K is necessary. Prothrombin deficiency can occur therefore in association with either gross liver disease or vitamin K deficiency. Naturally occurring vitamin K is an oil soluble substance, absorbed from the gastro-intestinal tract in the presence of bile It is a naphthoquinone and a water soluble analogue can be readily synthesised for the absorption of which bile is not necessary For the activation of prothrombin, two substances, or "plasma accelerators," Factor V and Factor VII, are needed, and deficiency of either of these also gives rise to interference and delay in the formation of thrombin from prothrombin. Interference with the prothrombin-thrombin reaction, or "hypoprothrombinaemia" *occurs in:*

1 SEVERE LIVER DISEASE, ATROPHY AND CIRRHOSIS.—These are conditions probably not greatly influenced by vitamin K therapy.

2 DEFECTIVE VITAMIN K ABSORPTION.—This results from [illegible] deficiencies [illegible] the bowel [illegible] newborn [illegible] of the vitamin from the gastro-intestinal tract in the absence of bile as in obstructive jaundice and biliary fistula These conditions can be corrected by vitamin K therapy.

3 COUMARIN POISONING.—In this condition, there is in addition to hypoprothrombinaemia, deficiency of Factor VII,[6, 7] and the response to vitamin K is variable, but vitamin K_1, the naturally occurring oil soluble product is more effective in the correction of the deficiency.

Ionisable calcium.—Ionisable calcium is necessary for the formation of thrombin but its deficiency is never a cause of delayed clotting in vivo, and even in the most severe degrees of this associated with hyperparathyroidism there is no demonstrable change in the clotting mechanism

Thromboplastin.—Although thromboplastin is a product to a certain extent of the disintegration of platelets, reduction of these in the blood has

to be extreme to affect the clotting time. In essential thrombocytopenia, Werlhof's disease, capillary bleeding is common but the bleeding tendency is not significantly correlated with the number of platelets, and the disease may be due not only to shortage of platelets, but also to capillary damage. The clotting time is in fact often unaffected in this condition. Thrombocytopenia also occurs as a result of acute infection and aplasia of bone marrow, or when the marrow is replaced by leukaemia or malignant tissue; and in susceptible individuals as a result of sensitisation to drugs such as sedormid,[8, 9] and in these conditions there is a bleeding tendency. Plasma which is free of platelets will still clot in the presence of damaged tissue cells, from which also a supply of " thromboplastin " can be obtained. Russel viper venom has a thromboplastin-like action and is used as a local haemostatic.

Fibrinolysis.—In order to remove fibrin formed in excess during the process of repair and haemostasis, there exists in the globulin fraction of normal plasma a fibrinolytic enzyme, plasmin. It is normally in a precursor state, and is activated by tissue extracts. There are other fibrinolytic enzymes present in the blood, which are liberated by exercise, emotion and possibly the administration of adrenalin.[12, 13] Excess fibrinolysins occur in ante-partum haemorrhage, sometimes after incompatible blood transfusions and after surgical operations, especially pneumonectomy, and they may be a cause of excessive bleeding.

HAEMOPHILIA

In haemophilia there is an inherited bleeding tendency in males, transmitted by females. Females can, very rarely, suffer from haemophilia but only if they are born of the union of a haemophilic male and a female carrier. Latins, but not Jews, appear to escape the disease.

Haemophilia has been shown to be due to absence or reduction of a plasma component necessary for the formation of thromboplastin known as the antihaemophilic globulin, a substance which is preserved in normal plasma kept solid by freezing[10] or dried lyophilically within a short time of collection[11].

Fifty ml of fresh plasma is often effective in restoring the coagulation time to normal for some hours, but the haemostatic mechanism is still grossly deranged, as can be shown by more specific laboratory tests The clotting time is a very crude index, and about one-third of haemophiliacs have a normal clotting time, but they still bleed abnormally. Operations should be avoided if at all possible, but if necessary about 1,500 ml. of *fresh* or specially preserved plasma every twenty-four hours are probably required to restore normal clotting. Expert knowledge and laboratory facilities should be available if operation has to be done. Certain coagulants used locally may help to control bleeding (p 604).

Abnormal bleeding first appears early in life, generally from a minor injury or scratch; after circumcision, tonsillectomy or extraction of a tooth;

or as haematuria, haematemesis, melaena, epistaxis, cerebral haemorrhage, haematoma formation or haemoarthrosis.

Bleeding occurs in attacks, between which clotting may seem normal, but laboratory investigation will always show that this is not so.

ANTICOAGULANTS

Any substance which interferes with the clotting of the blood is an anticoagulant Removal of calcium ions from the blood will prevent coagulation and such a method is in frequent use in the collection and storage of blood. The addition of sodium citrate or oxalate to drawn blood acts by the formation of a non-ionisable calcium citrate or insoluble calcium oxalate. Such methods are not suitable for therapeutic use, though sodium citrate is usually employed to prevent blood for transfusion from clotting.[14]

Heparin.—This substance was discovered by McLean in 1916 and a great deal of important work and research has been carried out especially in Toronto[15 16 17] and in Sweden[18] Heparin is, in large measure at least, an antithrombin and therefore acts on the last stage of coagulation by interfering with the thrombin-fibrinogen reaction It has a greater affinity for thrombin, than has fibrinogen, and thus thrombin is inactivated. Heparin is also to some extent an antiprothrombin. Unfortunately it is not absorbed unchanged from the gastro-intestinal tract and cannot be given by mouth, and therefore intravenous, intramuscular or subcutaneous injection is necessary. It produces its anticoagulant effect shortly after a single intravenous injection, an effect which decreases rapidly and within three or four hours [illegible]

[illegible] subcutaneous[19] and intramuscular[20] routes have been advocated and are effective though rather irregularly so. They are also painful but the pain can be prevented by previous injection via the same needle of 2 ml of a 2 per cent. solution of [illegible]

[illegible] slowly absorbed substances, *e g.* [illegible] menstruum, have been used to provide depôt treatment[21] but for like reasons their use has not become general

Scheme of dosage —Heparin should be used in such a quantity that the clotting time is increased from the normal four to eleven minutes to twenty or thirty minutes

The estimation of the whole blood clotting time (Lee and White)[22] —Several clean glass tubes $2\frac{1}{2}'' \times \frac{3}{8}''$ are required. After accurate venepuncture venous blood is rapidly withdrawn into a dry paraffin coated syringe. Into each of four tubes is put 1 ml of blood from the syringe, the temperature of

the tubes being kept constant at 37°C. preferably in a waterbath. The tubes are then tilted in turn at about $\frac{1}{2}$ minute intervals, and the time from withdrawal of blood until its solidification in the tubes is recorded. The average time in the four *tubes is considered the clotting time.*

The dosage which is used in Britain is based on the international unit, *one unit containing* $\frac{1}{130}$ mg. of a standard heparin. The international unit is almost the same as the "Toronto" unit.

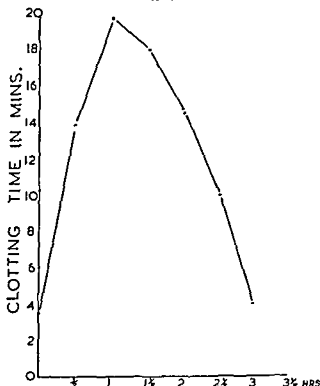


Fig. 326
This shows the short-lived anticoagulant effect of a single dose of heparin given intravenously.

As soon as anticoagulant treatment is considered necessary 12,500 i u are *given intravenously. Thereafter at four-hourly intervals 10,000 i u.* are given. In a small adult these doses are reduced by 2,500 units, and later adjusted according to the clotting time estimation. Many clinicians omit the night dose, but for the first two days at least we cannot agree with this practice as its omission means that for at least four hours there is little or no anticoagulant effect in the blood, and there is no adequate reason to suppose *that during* this time further clot will not form We therefore insist on the night dose. *It is advisable to obtain a clotting time an hour after* the first dose, and daily thereafter, and it is important that the estimation is done one hour after the heparin is given in order to obtain comparable records Occasionally considerably larger doses will be necessary in resistant patients, and sometimes the dose may have to be reduced, but not omitted, where the clotting time *exceeds thirty minutes. In order to avoid repeated* intravenous injections, a

polythene tube can be introduced into a vein and left *in situ*, and the drug given via a Gordh's needle inserted into this, without disturbing the patient (Fig 327).

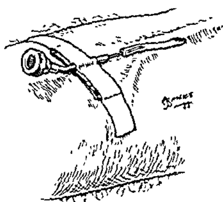


Fig. 327
Through a Gordh's needle inserted into a polythene tube in a vein heparin can be given without disturbing the patient.

Heparin can be rendered inactive by protamine sulphate, and injection of this in doses of 50-100 milligrams in a 1 per cent solution intravenously will neutralise the circulating heparin Other substances also inactivate heparin, among which is streptomycin; increased doses of heparin may be necessary

There are practically no toxic effects of heparin though occasionally anaphylactoid reactions are seen. Apart from this the only complication arising from treatment is haemorrhage. Haematuria, bruising, haemorrhage from an operation wound and sometimes petechial haemorrhages may occur, but there is no added risk of haemorrhage from heparin in the puerperium or during menstruation It is impossible to estimate the incidence of complications from haemorrhage occurring with heparin therapy but fatalities have occurred[23] We have not experienced a fatality, but we have seen very serious haemorrhage following an operation for peripheral vessel grafting, which was due, not to leakage from the anastomosis, but to general ooze from the long incision necessary for the operation. It was controlled by protamine sulphate.

Dextran sulphate.—Heparin is the sulphuric ester of a complex poly- saccharide Dextran is a polysacch... certain molecula...

... withdrawal ... results in return of clotting time to normal within six hours, and its effect in an emergency can be stopped by means of protamine sulphate It differs from heparin in its clinical action to the extent that a six-hourly intravenous dose is as effective in prolonging the clotting time as is a four-hourly dose of heparin, and therefore its use is less disturbing to the patient A further advantage is that it is a synthetic substance and therefore more easy to standardise than a biological product like heparin. Clinical trials have been made in Birmingham, Edinburgh, Glasgow and the Post-graduate Medical School, London, and there have been no toxic effects. It appears to be as effective clinically as heparin.

The coumarins.—The coumarins were ... (1941)... from ...

disease of cattle. This group of substances ("dicoumarol," "tromexan," "dindevan," etc.) acts by preventing the formation of prothrombin and factor VII in the liver. A reduced "prothrombin" content in the blood results in impaired clotting and less effective thrombus formation. They are readily synthesized and are active after oral administration, thus having a great advantage over heparin, but in view of the fact that they have to be absorbed from the gastro-intestinal tract, their action is slow. In the case of dicoumarol the full effect may not be reached for forty-eight or seventy-two hours, but with tromexan or dindevan the period is halved. Estimations of clotting time are valueless in the control of these drugs, and estimation of "prothrombin" in the blood is necessary. The prothrombin index, a measure of "prothrombin" activity, should be reduced to 40 - 50 per cent. and maintained at this level

THE ESTIMATION OF PROTHROMBIN INDEX IN THE BLOOD.—For the estimation of prothrombin, the one-stage method of Quick should be used. In this test the clotting time of normal plasma is obtained and divided by the clotting time of the patient's plasma, the result being expressed as a percentage. This is known as the "prothrombin index," but in actual fact it has little to do with the prothrombin content of the blood, being merely a guide to the activity of this complex.

Method.—0·1 ml of undiluted normal oxalated plasma is added to 0·1 ml of brain emulsion, a source of thromboplastin, and the mixture is warmed to 37°C in a water bath. 0·1 ml. of M/40 calcium chloride, warmed to 37°C., is then added rapidly from a graduated Pasteur pipette and the coagulation time is recorded from the time of addition of the calcium. The test should be made in triplicate and the mean of the three readings recorded. The same procedure is repeated with the patient's plasma.

There are other methods of estimating and recording "prothrombin" activity in the plasma, and this may lead to confusion. It is better to become familiar with one method to avoid errors in the use of coumarin drugs

The usual dose of dicoumarol is 300 mg., 200 mg. and 100 mg on the first three successive days, the dose being regulated thereafter by the prothrombin estimation. Tromexan is given in amounts of 1·2 gm., 0·9 gm. and 0·6 gm on the first three successive days, and it is preferable to divide the doses. With both drugs daily estimations of the prothrombin are necessary for regulation of the subsequent daily dose. In our experience we prefer Tromexan owing to its quicker and less sustained action which allows a greater margin of safety than is the case with dicoumarol. It is essential to continue the daily estimation of the prothrombin at least for four days when the tolerance of the patient will be evident and after this bi-weekly estimations should suffice

Haemorrhage from the use of dicoumarol has frequently been reported, and has on occasions been fatal Nicol (1950)[28] reported a death rate of 0·18 per cent. in 18,500 cases We have seen subarachnoid haemorrhage result from over-dosage with dicoumarol. Such accidents are preventable and should

not occur if the dosage is carefully controlled. The action of the coumarins can be stopped by means of a fresh blood transfusion which may have to be repeated after six hours owing to the contained prothrombin and other factors of the first transfusion having been used up—a prothrombin index estimation will indicate this. At the same time vitamin K_1 in 5 per cent. solution should be given in doses of 500 mg. to 1,000 mg. and this should be repeated, together with the blood transfusions, until the prothrombin index has risen to 50 per cent. Only the requisite *minimum* of vitamin K_1 should be given because if the prothrombin is significantly raised it may be difficult with the courmarins subsequently to achieve an anticoagulant effect for a week or so and it will be necessary to change to heparin. It should be noted that vitamin K_1 may require four to six hours to achieve its effect, and prothrombin estimations should be done at least six hours after administration of the drug.

Vitamin K_1 is available in solution for injection under the trade name of Mephyton (Merck) and as an emulsion for oral administration, Konakion (Roche).[29] Bile salts are not necessary for its absorption when it is emulsified.

Many of the failures of transfusion and vitamin K to stop haemorrhage in coumarin poisoning have occurred because they have not been given in sufficient quantity nor over a sufficiently prolonged period.

Contra-indications to anticoagulants.—Anticoagulants should be avoided in liver disease and jaundice, advanced kidney disease, gastro-intestinal bleeding and subacute bacterial endocarditis. They should be used with great caution and with certain safeguards (*see* p. 813) after arterial grafting or vascular anastomoses, and are in fact probably unnecessary. They should be avoided for twenty-four hours after any operative procedure within the cranium and thoracic cavity, and generally speaking within the abdominal cavity.

Standard anticoagulant treatment.—In order to achieve rapidly an effective anticoagulant level of the blood, heparin is given immediately. At the same time Tromexan is given to reduce the prothrombin index of the blood, and when this is reduced to 40-50 per cent. of normal, heparin injections are stopped, the anticoagulant level in the blood being maintained by Tromexan. An intravenous injection of 12,500 units of heparin as an initial dose and 10,000 units four-hourly thereafter is given. During the first day of treatment 1.2 gm. Tromexan is given by mouth in two doses of 0.6 gm. Twenty-four hours after starting treatment, a clotting time and prothrombin index is obtained, and if the latter indicates a level of 45 per cent. or less, injections of heparin can cease, but if above this level, heparin must be continued for another day, in doses regulated to maintain a clotting time of twenty minutes. On the second day of treatment 0.9 gm. Tromexan, in divided doses is given. The prothrombin index is repeated on the third day, and the dose of Tromexan regulated accordingly with the object of maintaining the prothrombin index

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at 40 - 50 per cent. Once the dosage of Tromexan is established prothrombin estimation need be made only on alternate days, or even twice a week in cases where the treatment is to be prolonged.

COAGULANTS.

There are no known therapeutic substances which can be injected into the blood stream to increase the coagulability of the blood, except when there is some specific defect in the clotting mechanism to be corrected, such as occurs in deficient absorption of vitamin K in the presence of obstructive jaundice, etc.

Locally applied haemostatics consist of those which clot fibrinogen, and those which promote thrombin formation.

A number of substances can clot fibrinogen, but for clinical use thrombin from the ox, rabbit or man is the most important. It can be used in conjunction with a fibrin foam, when an effective haemostatic agent is formed, which is absorbed without any delay of the healing process.

Those substances which promote the formation of thrombin by a thrombokinase-like action include many tissue extracts and snake venoms Russell viper venom is particularly effective, and has a very powerful action but requires calcium for its full effect. It is effective in very dilute solution even when many million times diluted, an important consideration when a locally applied coagulant may be considerably diluted by further bleeding, e g. in a prostatic cavity

Local treatment of haemorrhage from a wound occurring in a haemophiliac.—Russell viper venom or thrombin combined with absorbale fibrin foam will often arrest haemorrhage in these circumstances. The wound surface should be cleaned of blood and the fibrin foam, impregnated with one or other of these local haemostatics, is then applied with pressure, in order that the dressing be not immediately floated off. The pressure must be relaxed at frequent intervals to avoid necrosis of the underlying wound

P. M

3. NEOPLASTIC INVASION OF VEINS.

4. IN VARICOSE VEINS.

2. Thrombosis due to *alterations in the physico-chemical constitution of the blood*

1. In association with distant malignant disease, especially of the pancreas, but also of stomach and lung

2 As a complication of infections and fevers—typhoid, pneumonia, septicaemia and almost any kind of acute infection.

3 In association with blood disorders—polycythaemia rubra vera, secondary polycythaemia, leukaemia and perhaps certain anaemias.

3. Thrombosis associated with stasis of the blood stream

Venous stasis by itself is probably not a cause of thrombosis, but if in addition there is intimal damage and/or some physico-chemical change in the blood, thrombosis is frequent Decubitus thrombosis[6] has been suggested as a term for this condition

1. TRAUMA

(*a*) **Direct *injury to veins*.**—In all open wounds, whether resulting from injury or operation, thrombosis of damaged veins occurs. It is generally localised to a remarkable degree as a result, in some measure, of the action of circulating fibrinolysins[7] which remove clot that is surplus to requirements. Sometimes thrombosis spreads and may occasionally [illegible]

[illegible] operation area, but to post-operative or decubitus thrombosis in the veins of the leg In lacerated wounds without infection, extensive thrombosis is rare, unless as a result of the injury a period of bed rest is necessary; other factors then become operative. Intravascular thrombosis may occur as the result of a closed injury, but in the majority of cases it is self-limited and localised A simple muscular strain or bruise may also be followed by thrombosis which may involve a particular group of muscles, a single muscle, or even part of a muscle, giving rise to a localised, sometimes persistent, swelling of the injured muscle or part of the muscle In these rare cases pain often resembling that of intermittent claudication develops, probably because the degree of venous thrombosis is sufficient to interfere with the efflux of blood from the muscle affected and thus with its nutrition Although [illegible] in girth at the site of the inju[illegible] limb such as would be present [illegible] of the limb were thrombosed. We have recently seen this in a policeman who was struck on the leg by the bumper of a car with consequent swelling of the calf muscles. After a period of rest in bed the swelling partially subsided but he then suffered pain after walking a short distance This was eased by a few minutes rest

CHAPTER XX

VENOUS THROMBOSIS AND EMBOLISM

IN 1784 Hunter[1] under the title "Observations on the Inflammation of the Internal Coat of the Veins" drew attention to thrombosis following venepuncture, compound fractures and operations. He noted the association of infection, inflammation of the vein wall and subsequent thrombosis, but some cases which occurred when there was no apparent suppuration he referred to as "spontaneous inflammation of the vein wall." He considered that local inflammation was the essential factor, and that contiguity to an acute infective process was usual. His views were supported by Cruveilhier.[2]

Venous stasis as an important factor in thrombosis was incriminated by Virchow[3] in 1860. Rokitansky[4] thought that two varieties of thrombosis occurred, one following inflammation of the vein wall, and one resulting from venous stasis. Welch[5] in 1898 reviewed very fully the whole subject, and concluded that there was more than one factor responsible in most cases, and that neither inflammation nor stasis was alone responsible for many.

Two distinct clinical conditions are now recognised—simple venous thrombosis, and venous thrombosis associated with an inflammatory reaction of the vein wall, but it is generally agreed that in most instances these are stages of the same pathological process, and are not distinct diseases. They will therefore be discussed together, although the appreciation of the different *clinical and pathological features of simple venous thrombosis*, or phlebothrombosis, and the later stage of the same disease process with inflammation of the vein wall, or thrombophlebitis, is helpful in the understanding of the condition.

CAUSES OF THROMBOSIS AND THROMBOPHLEBITIS

1. *Thrombosis due to intimal damage*

1. TRAUMA

(*a*) Direct injury to veins, bruising and laceration

(*b*) Indirect injury to veins—tramautic axillary vein thrombosis and thrombosis in the popliteal vein after effort.

(*c*) Thermal and chemical injuries.

2. *INFLAMMATION*

(*a*) Acute inflammation of the vein wall by extension from neighbouring acute infective processes.

(*b*) Non-suppurative inflammatory lesions, thrombophlebitis migrans and thromboangiitis obliterans.

cation of blood disorders such as polycythaemia vera, cardiac failure, invasion of or compression by enlarged glands secondary to carcinoma of the breast or lung, mediastinal tumour and aneurysm, but these causes of thrombosis are excluded by the physical examination of the patient, the blood count and radiology of the chest. We have seen thrombosis of the axillary vein occurring in a man six years before the onset of thromboangiitis obliterans.



FIG. 329



FIG. 330

FIGS. 329 and 330 The venogram shows absence of filling of the axillary vein and filling of tortuous distended collateral veins

Although symptoms tend to improve after a few days, and may completely disappear, there is a tendency for pain to recur after use and for swelling to persist, sometimes varying in intensity from time to time, but often interfering severely with occupations that require active use of the affected arm.[13, 14] Pulmonary embolism is not recorded as a complication of primary axillary vein thrombosis

The aetiology of the condition is not clear. Compression of the vein between the clavicle and the first rib,[15] pressure on the vein by the pectoralis

Deep venous thrombosis frequently occurs when a period of immobilisation or bed rest has been necessary after injury, especially after a fracture,[8] but also after a sprain or even a trival injury of the leg. Whether this results from thrombosis in continuity from the site of the injury, or whether the mechanism is similar to that of post-operative thrombosis is difficult to say, but in its clinical course it resembles the latter.

(*b*) **Thrombosis from indirect injury of the vein wall.**

AXILLARY VEIN THROMBOSIS SYNDROME OR TRAUMATIC AXILLARY VEIN THROMBOSIS.—The former title is preferable because there is sometimes no thrombosis of the vein, but obstruction of the lumen. The condition was first described by Paget in 1875.[9] It usually occurs in men and as a result of some unaccustomed effort and is seen therefore most commonly in the right arm and at any age, although the age group twenty to thirty is most commonly affected.[10, 11] The type of movement which appears to be responsible is often rotation against resistance with the arm fully abducted, such as turning a screwdriver with the arm above the head, but any repeated movement with the shoulder in full abduction, painting a ceiling for example, may cause it. Sometimes the effort is slight and almost insignificant[12] and in 10 per cent. of cases a swollen arm has been first noticed on waking in the morning. The syndrome is characterised often by the sudden, but occasionally by the gradual, onset of venous obstruction of the arm, with a non-pitting swelling of the limb from the fingers to the shoulder. The whole limb may be cyanosed and occasionally mottled in appearance. The axillary vein is usually felt as a tense palpable cord and the subcutaneous veins are distended and visible (Figs. 328 to 330), but the neck veins are not affected—proof that the thrombosis does not involve the innominate veins. Pain varies in severity, but is generally in the nature of a dull ache, situated more in the shoulder region than in the distal part of the limb, and accentuated after use of the limb. Sometimes pain is absent. It has frequently been observed that the hand on the affected side is cooler. Venography is of some value in diagnosis showing obstruction of the axillary vein, the blood being conveyed by the cephalic vein and other collateral veins, enlarged considerably and often tortuous, particularly in long-standing cases. Thrombosis of the axillary vein may occur also as a compli-



FIG. 328
Collateral veins are clearly seen There is no distension of neck veins

Even if, as Hughes suggests, some cases are the result of a ligature-like action of a pre-venous phrenic nerve, it is evident that not all can be so explained, and it may be that there is more than one cause for the condition.

TREATMENT

Conservative treatment, rest and elevation together with anticoagulant therapy, should be tried initially if the patient is seen in the earliest stages. These measures are generally accompanied by relief of symptoms, the collateral veins enlarging. Physiotherapy may be of benefit. If symptoms persist, surgical measures may be considered, but no one method appears to be universally effective. In one reported series resection of the axillary vein was performed without benefit, but in no case was the proximal end of the thrombus reached.[12] Scalenotomy has been reported as successful.[22] Thrombectomy has been suggested but would hardly be applicable if no thrombosis were found and would almost certainly be followed by further thrombosis. Sympathetic block[23] is successful sometimes in relieving symptoms particularly when the hand on the affected side is cooler, it acts probably by blocking a nervous reflex and by assisting in the dilatation of collaterals. If swelling, pain and venous congestion persist, it has been suggested that a venous anastomosis between the subclavian vein, if it is patent, and one of the jugular veins might be performed.[10] It does not seem that surgical treatment has much to offer, the aetiology is so obscure, but in those patients who have obj... ly a cooler ... companied ... In one of ... marked improvement, with reduction of swelling and disappearance of pain for eighteen months, after which the pain recurred.

EFFORT THROMBOSIS AND "IDIOPATHIC" THROMBOSIS OF THE DEEP VEINS OF THE LOWER LIMBS.—Thrombosis of the deep veins of the leg occurs in otherwise healthy people. It may be associated with a sudden "effort" of the leg, such as a twist or recovery of balance from a trip or slip, although it frequently occurs without apparent injury or strain. It is unprofitable to attempt to separate effort thrombosis from idiopathic thrombosis for in the latter it is impossible to exclude a minor strain.

Of 133 ... at Ham... an incid... between twenty-five and seventy-six and ...e were twelve females to seven males. On the other hand presumably many cases of idiopathic thrombosis of the deep veins of the leg do not find their way into hospital if they suffer no symptoms apart from a little gravitational swelling. It has ... thromb... ... with the legs crossed and ...neys by car and aeroplane when stasis aggravated by pressure behind the knees or the popliteal veins might be assumed.[23] A number of cases

minor,[16] by the costocoracoid ligament,[17] by the subclavius muscle[18] and by the subscapularis[19] have all been advanced as aetiological factors. Gould and Patey[18] considered that damage to the subclavio-axillary valve with subsequent thrombosis at this site was the cause. Recently Hughes[10] in an excellent review of the subject concluded that no one type of movement was always responsible for the onset of symptoms and that therefore no single theory could account for all cases. Furthermore surgical exploration has not revealed a thrombosis to be in fact present in all cases, as it would be if intimal damage was the cause. From a series of anatomical dissections he concluded that a pre-venous phrenic nerve, an anatomical arrangement occurring in 4 per cent. of all subjects,[20] exerts a ligature-like action on the subclavian vein as it passes in front of the tendon of the scalenus anterior muscle, and as the excursion of the right side of the diaphragm is greater than the left[21] the right phrenic nerve is drawn more tightly than the left, which would explain the more common situation on the right side than the left (Fig 331). Furthermore, deep breathing and extension of the neck are accompanied by contraction of the scalenus anterior and this causes further obstruction of the vein. Deep breathing is sometimes an important factor in the production of symptoms; some cases have been reported as appearing for the first time on waking up in the morning, when the patient yawns or sighs with the neck hyperextended

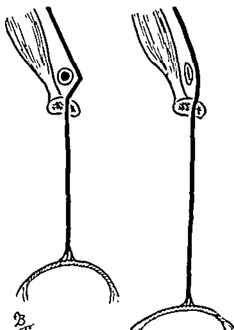


FIG. 331
Contraction of the diaphragm leads to traction on the phrenic nerve. This constricts the subclavian vein as it passes in front of scalenus anterior (*After Hughes.*)

Thrombosis of the axillary vein sometimes extending upwards to involve the subclavian vein has often been found at exploration,[12] but on the other hand there has sometimes been no thrombosis. It would seem therefore that the obstruction to the vein which is undoubtedly present must be due, in the latter cases at least, to pressure on the vein by some structures, perhaps indeed a pre-venous phrenic nerve, which acts like a ligature Such a mechanism would explain the absence of embolic phenomenon.

Of five cases recently seen by us three have occurred in males, two in females. One was explored and the axillary vein was found to be thrombosed up to a point behind the subclavius muscle, but there appeared to be no undue pressure on the vein by the muscle or by any other structure The subclavian vein was free from clot. The phrenic nerve was found to pass in its usual relationship between the subclavian artery and vein

Homans[27] described four cases of venous thrombosis, three appearing after minimal injury and affecting the main veins below the knee; two of the patients died of pulmonary embolism. Before the fatal incident their symptoms consisted of slight swelling and cyanosis which completely disappeared after rest in bed. A post-mortem examination in one of the fatal cases revealed a pulmonary embolus 15·5 cm. long, and exactly fitting the popliteal vein, that had originated apparently in the veins of the calf muscles. Homans recommends that when a diagnosis of idiopathic or effort thrombosis of the veins of the leg is made, embolism is sufficiently probable to justify prophylactic ligation of the femoral vein. Evoy[28] in a review of 1,000 cases of fatal pulmonary embolism collected from the literature stated "severe muscle or ligament strain seemed to create and foment the thrombosis."

Pulmonary embolism occurred in seven out of nineteen or 36·7 per cent. of our cases of idiopathic popliteal thrombosis whereas in 114 cases of other forms of thrombosis of the leg veins 29 per cent. developed embolism, a difference which is insignificant. If it is admitted that a large number of effort or idiopathic thromboses never reach hospital, the fatality rate of all cases must be small, and the risk of embolism does not seem so great as to demand immediate ligature of the femoral vein. The condition should certainly be treated in the early stages by anticoagulants, and if pulmonary emboli occur in spite of this therapy, then ligature of the superficial femoral vein might be considered.

(c) **Thermal and chemical injuries.**

1 THERMAL INJURIES.—Intravascular thrombosis may occur as a result of *direct injury* by *burns* or *frostbite*.

2 CHEMICAL INJURIES.—Almost any intravenous injection may result in thrombophlebitis of the vein into which the injection is made. [illegible] drugs [illegible] use [illegible] but [illegible] polythene tube frequently result in venous thrombosis.

Blood and plasma transfusion are frequently followed by [illegible] recipient vein [illegible] is often ass[illegible] weeks and [illegible] blood or blood substitutes are given for haemorrhage or shock they should be given rapidly, preferably with a suitable transfusion pump[29] in order to restore the blood volume as soon as possible, for when the infusion is not prolonged local thrombosis rarely occurs. If transfusion has to be prolonged for any particular reason—in some cases of anaemia for example—the addition of heparin, 5 units per ml. of the blood or blood substitute to be given, will prevent local thrombosis.[30]

Therapeutically the intima of the veins is deliberately damaged by the injection of various chemicals as in the treatment of varicose veins and

were recorded in persons after spending the night on a camp chair in an air-raid shelter during the war, and deaths from pulmonary embolism in such have resulted.[26]

The thrombosis is generally of sudden onset, and has occasionally been accompanied by a severe pain described as being like a blow on the calf with a stick, rather similar to the pain of ruptured plantaris tendon.

A woman, aged fifty-five, was walking from one room to another in her house when she felt as though she had been struck on the calf of the left leg with a stick The leg was tender and painful, but she did not consult her doctor and went to bed for the next few days, during which the pain gradually eased. Five days after the incident she resumed her normal household duties to find that the leg was swollen at the end of the day, returning to normal during the night. She was seen about a fortnight after the incident when the left leg from the knee downwards was found to be considerably swollen, with pitting oedema extending to the dorsum of the foot, and a cyanotic tinge of the foot. All distal pulses were normal



FIG 332
Idiopathic thrombosis of the deep veins of the left leg. It is only the history that suggests the thrombosis is idiopathic.

Usually the onset is painless and the swelling, which occurs at the end of the day and which is often of minor degree, is well tolerated until finally the patient presents a post-phlebitic leg or a gravitational ulcer. Idiopathic thrombosis of the deep veins may well be an important cause of post-phlebitic syndrome (Fig. 332).

We have recently seen three males, aged forty-two, fifty-three and sixty-two, admitted to hospital with pain in the chest, haemoptysis and X-ray appearances consistent with pulmonary embolism. In each of these examination revealed deep thrombosis of the leg veins which, judging from the history, had occurred spontaneously from eight to twenty-one days previously

A further patient who probably died from pulmonary embolism was a male aged forty-two. He complained of pain and swelling of sudden onset in the left leg. On examination the left leg was swollen below the knee, and there was tenderness in the calf muscles. His general condition was good and there was no apparent cause for thrombosis Admission to hospital was advised, but this he refused, preferring to rest at home Anticoagulants were consequently not given We were told that he died suddenly in his office chair ten days later. The mode of death was consistent with massive pulmonary embolism

onset of arterial obstruction or Raynaud's phenomenon by periods of from two and a half to twenty years; one patient in whom biopsy of an affected vein revealed evidence of thromboangiitis obliterans has not yet developed evidence of arterial insufficiency after eleven years; four have occurred in association with carcinoma, one of the stomach, one of the breast and two of the body of the pancreas. Migrating thrombophlebitis has also been reported in association with carcinoma of the lung and gall bladder, but it appears that the body or tail of the pancreas is the site of the carcinoma in 60 per cent. of cases of this association



FIG 333

Multiple patches of superficial thrombophlebitis can be seen, and felt, in both thighs This patient had absence of one posterior tibial pulse, and section of an inflamed vein revealed appearances consistent with thromboangiitis obliterans

It is probably true to say that the distal veins of the leg or arm tend to be the site of the disease in thromboangiitis obliterans, and the larger leg and arm veins to be the site in malignancy, but this is not invariably so

In a recent paper on the subject one of us[33] has re-emphasised that histological examination of the biopsied veins may be a useful diagnostic aid in differentiating between the phlebitis which is a manifestation of thromboangiitis obliterans and that seen as a complication of malignancy. In the former there is characteristic perivenous and venous inflammation, whereas in the latter the thrombosis is bland and non-inflammatory (Figs. 334 and 335).

The cause of the association of phlebitis with cancer is not known Cultures of the vein are sterile Release of [illegible]

blamed [illegible]

[illegible] cells has been suggested as a [illegible] it is noteworthy that the thrombosis in such cases is not controlled by anticoagulants, which would appear to indicate that alteration in the composition of the blood is not an important factor.[34]

occasionally deep vein thrombosis results from this therapy even in the best hands.

2. Inflammation

(*a*) **Acute suppurative phlebitis.**—This is unusual as the veins, in common with other blood vessels seem to have considerable resistance to acute infective processes.

It may occur:—

(i) In superficial thrombophlebitis and transfusion phlebitis. In the former there is usually a leg ulcer, from which presumably the infection arises.
(ii) In the portal system in some cases of intraperitoneal suppuration.
(iii) In the pulmonary veins in the presence of suppuration in the lungs.
(iv) In lateral sinus thrombosis complicating mastoid infection.
(v) As a complication of pyogenic osteomyelitis of the long bones.
(vi) Occasionally in the pelvic veins in the presence of suppuration in the pelvis.

Suppurative phlebitis is serious and often fatal from infected emboli, and proximal vein ligation, if practicable, should be performed.

(*b*) **Thrombophlebitis migrans and thromboangiitis obliterans.**—Thrombophlebitis migrans or recurring superficial thrombophlebitis, first described by Frémy in 1864,[11] is an uncommon condition and is evidence of thromboangiitis obliterans or rarely visceral cancer. Whether the condition occurs idiopathically is to be doubted as attacks of phlebitis may occur sporadically for many years before the disease of which it is a symptom becomes manifest It occurs generally in males with an average age of forty years, and the history is longest when it is associated with thromboangiitis obliterans, and shortest when it is associated with malignancy. The phlebitis occurs usually in the lower extremities, less commonly in the upper extremities, and gives rise to pain, redness and swelling of a short segment of vein (Fig 333). Veins at multiple sites may be simultaneously affected, both legs being involved or an arm and a leg. There is sometimes fever and toxaemia; sometimes no general reaction. After two to three weeks the inflammation subsides leaving a firm, isolated painless swelling of a segment of vein The attacks occur at intervals of weeks to years and are *characteristically episodic*, and there may be seen in one patient phlebitis at varying stages of activity, *in one place developing, and in another resolving.*

Pulmonary embolism has been reported,[12] but we have not seen this complication. It seems probable that in cases secondary to visceral cancer deep vein thrombosis occurs in a proportion from prolonged bed rest, and it may well be that the pulmonary embolism originates from these deep veins and not from the superficial veins.

Of twelve of our patients who suffered from recurring thrombophlebitis, seven later developed thromboangiitis obliterans and the phlebitis preceded the

In no case where malignancy has been the primary factor in the condition, has surgical treatment of this resulted in relief from attacks of phlebitis.

There is no specific treatment, whatever the underlying factor, but a biopsy should always be done with a view to determining the presence of thromboangiitis obliterans, the commonest cause. Should this measure reveal the presence of simple thrombosis, then if this is recurring and superficial, a most careful search should be made for malignancy, and such a search demands all methods available including perhaps even laparotomy, provided malignant disease of the lung has been excluded.

3. Neoplastic Involvement of Veins

The walls of the longer blood vessels appear to be very resistent to invasion by malignant disease, but where this does occur, venous thrombosis results Venous obstruction and thrombosis may result from pressure by a tumour from without, there being no actual invasion of the vessel walls

4. In Varicose Veins

Localised

of

of … it may appear without apparent cause. Presumably trauma damages the intima of a vein already abnormal, resulting in thrombosis The internal or *rarely the external* saphenous system is affected, and the lesion often remains localised, although it may spread up and down the main trunk of the saphenous vein. *Clinically*, there is pain, tenderness, redness and swelling in the region of the affected vein, and swelling involving the whole limb which may be quite severe. There is often a mild pyrexia. The condition resolves over the course of *a week or two*, leaving an indurated painless cord palpable in the limb though rarely suppuration may occur particularly where there is an ulcer of the leg Apart from these rare cases the inflammatory reaction in the vein wall is uninfected, and results in firm fixation of the intraluminal clot There is *no risk of the clot moving* to form an embolus. However, the thrombosis may build up *a "tail" of clot* which may extend some inches, and may even overflow into the femoral vein, where it may break off and form an embolus, though a small one, or alternatively become adherent to the femoral vein, giving rise to *obstruction* of this vessel In patients with ascending saphenous phlebitis, it is our practice to explore the sapheno-femoral junction if and when the clinical signs of thrombophlebitis reach mid-thigh, and we have repeatedly found a tail of clot not adherent to the vein wall in the upper part of the saphenous vein, sometimes extending into the femoral vein for some inches It is interesting to note that the saphenous vein in the upper thigh *in such* cases is not tender nor is it palpable until such time as the contained clot becomes adherent to the walls of the vessel when the local signs of thrombophlebitis appear. In fact the clinical and operative findings

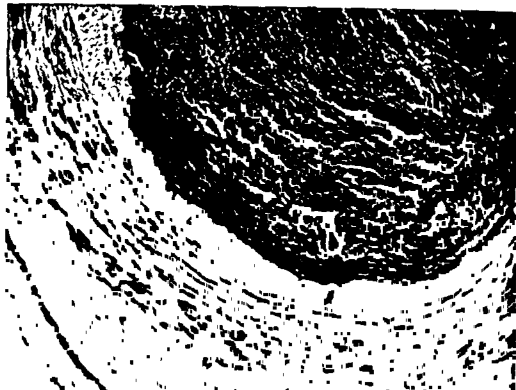


FIG. 334
Thrombophlebitis migrans in a patient with carcinoma of the pancreas. There is no inflammatory reaction in the wall of the vein.



FIG. 335
Thrombophlebitis migrans in a patient with Buerger's disease. There is a marked inflammatory reaction throughout the vein wall.

tions,[36] revealed multiple venous thromboses in 5 of 16 cases of carcinoma of the body or tail of the pancreas, and in only 3 of 31 cases of carcinoma of the head of the pancreas, whereas there were only 2 of 81 cases of carcinoma of the stomach. Other series have been

... of 147 with ...

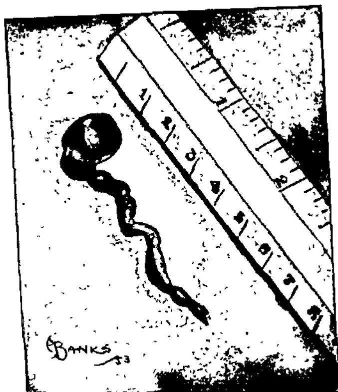


FIG. 337

The tail was lying in the lumen of the femoral vein and the "head" in a saphenous varix The "head" was continuous with adherent clot in the saphenous vein, and clinically superficial thrombophlebitis was present up to the saphenous opening

The thromboses affect the superficial and the deep veins, and in two cases associated thrombotic vegetation on the heart valves has been recorded.[39] There are occasional arterial thromboses and we have seen a patient with carcinoma of the body of the pancreas in which autopsy showed recent thrombosis in one brachial and one femoral artery, and multiple superficial and deep venous thromboses.

There is no known biochemical or other cause for the association; the possibility of an enzyme secretion which might alter the coagulability of the blood has been considered, but without being proved There is some reason

in these cases are a precise picture of proximal "phlebothrombosis" and distal "thrombophlebitis" as they occur in the deep veins (*Fig. 336*).

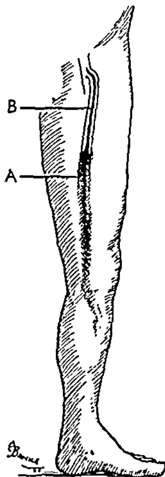


FIG. 336
Superficial thrombophlebitis
At A there is pain, tenderness, swelling and redness, at B there is no pain, no tenderness and no swelling, but the vein contains clot and this cannot be felt on examination

If therefore there is tenderness and a palpable vein half-way up the thigh, it is a matter of some urgency to expose the sapheno-femoral junction, incise the saphenous vein wall *and extract any clot* which may be present.

A man, aged forty-three, had suffered from primary varicose veins for many years. He developed *a phlebitis in the veins of the leg which* spread up to the mid-thigh. An emergency operation was done, and a clot arising in the saphenous vein and "overflowing" *into the femoral vein* was abstracted (Fig. 337) *It* was attached by its base to the adherent clot in the lumen of the saphenous vein, but not to the walls of the vessel *above this level.*

When a *distal phlebitis does not* extend proximally, the patient should be encouraged to remain up and active. Bed rest results in stagnation of blood and encourages further extension of the *thrombosis, or even deep vein thrombosis.* The limb should be supported by an elastic bandage to collapse the veins and so discourage consequent fresh thrombosis.

Sometimes a segment of superficial vein the seat of phlebitis will fail to resolve for some weeks. In these circumstances excision of the inflamed *segment of vein may be considered.* Occasionally suppuration occurs, and incision and drainage must then be done.

The superficial veins in the region *of a* gravitational ulcer or of a patch of dermatitis frequently become thrombosed with increase of pain, redness, tenderness and spread or development of *ulceration*

Thrombosis due to alterations in the physico-chemical constitution of the blood

In a large number of conditions where intravenous thrombosis is common, *the fact that there must be some alteration* in the constituents of the circulating blood appears inescapable, yet the nature of the changes is not understood.

Some change can be presumed in the following conditions

1. IN ASSOCIATION WITH INTRA-ABDOMINAL MALIGNANCY —In some cases of intra-abdominal cancer, *not only migrating superficial* thrombophlebitis, but also multiple deep thromboses may occur. This association was first described by Trousseau.[35] Sproul's analysis of 4,258 consecutive post-mortem examina-

patients not treated by early ambulation or exercises and the very earliest and mildest cases were detected. It is interesting to note that the same author quotes an incidence of 3 3 per cent in a second period under review when early rising after operation, together with ward exercises, was routine practice. Although statistical surveys have been made to a large extent on surgical and puerperal cases, thrombophlebitis is very much more common in medical practice, particularly in patients with increased venous pressure. Out of 114 in-patients with thrombosis at Hammersmith Hospital, excluding gynaecological and obstetric patients, the distribution was as follows:—

Cardiac disease	33
Pulmonary infections	13
Pulmonary neoplasm	8
Polycythaemia	4
Other blood diseases	4
Diabetes	4
Other diverse medical conditions	11
Peripheral vascular diseases	5
Post-operative	21
Infections and injuries of the limbs	11

Thus it is noted that only 21 out of 114 or 18 per cent. occurred after operation, whereas 54 out of 114 or 46 per cent. occurred in the course of cardiopulmonary disease.

The more the staff of a unit is "thrombosis-conscious," the more frequently is the condition diagnosed, and from a cross section of the literature and from our own experience it would appear that about 4 per cent. of patients develop detectable calf thrombosis after operation.

Factors Contributing to Thrombosis of the Leg Veins

Stasis.—There is no question that the stasis of bed rest from whatever cause is a major factor in venous thrombosis in spite of the fact that many invalids spend a great deal of their lives bedridden without developing manifest thrombosis, and that post-operative thrombosis is not abolished by rising on the day of, or the day following, operation Stasis of blood flow is encouraged by anaesthesia, post-operative sedation, and disinclination on the
patient to move on
by lack
excursio
... of the Fowler's
position ... of the knees and hips obstructs the main venous channels The importance of muscular action in maintaining the venous circulation in the limbs is perhaps illustrated by the following case.

A male patient, aged sixty-seven, underwent operation for severe intermittent claudication of the calf muscles. A unilateral tenotomy of the tendo Achillis was done with the effect of abolishing muscular action in the calf muscles. The patient began walking exercises the following day. He developed thrombosis in the treated leg and a minor pulmonary embolism occurred on the fifth post-operative day

to incriminate emboli of malignant cells[34] which do not survive, but which initiate thrombosis, although such cells cannot be demonstrated histologically in the thrombosed veins.

2. COMPLICATING INFECTIONS.—Although a complicating thrombosis is seen after many feverish illnesses, it will be appreciated that these fevers often impose prolonged recumbancy in bed, and thus the factor of stasis is introduced. In typhoid and pneumonia the thrombosis occurs about the fourteenth day of the disease, but it is said that it occurs much earlier in some other infections, especially influenza and acute tonsillitis, and it may be that in these there is in the blood some factor, still unknown, which precipitates thrombosis Haemoconcentration resulting from vomiting and diarrhoea may increase the coagulability of the blood—intracranial sinus thrombosis is not uncommon in dehydrated infants

3. IN ASSOCIATION WITH BLOOD DISEASES.—In polycythaemia vera and in polycythaemia secondary to emphysema or congenital heart disease there is a greatly increased red cell and platelet count, and a decreased clotting time, and venous and arterial thromboses are distinctly common. In primary polycythaemia there is a tendency for intestinal veins to be affected, while in polycythaemia secondary to congenital heart disease the cerebral venous sinuses are not infrequently the site of thrombosis.[40]

In anaemias and leukaemias the association is less clear, and probably thrombosis when it occurs is significantly aggravated by recumbency during the course of treatment.

Thrombosis associated with stasis. Decubitus thrombosis

This is the commonest and clinically most important variety of venous thrombosis, and is responsible for a large number of deaths, and a vast incidence of lung and leg morbidity. Few uncomplicated cases come to autopsy and post-mortem findings only give a picture of its incidence in the terminal stages of disease Robertson[41] reported calf thromboses in 47 per cent of medical and surgical autopsies, and this is about the mean percentage of most post-mortem reports The recorded incidence of thrombosis of leg veins, following confinement, operations or bed rest, depends on the recognition of the earliest and mildest cases by a careful clinical examination Until the last decade such signs and symptoms had not been generally recognised. Bauer[42] collected statistics from continental clinics and found that 2,874 of 178,252 operations were followed by thrombosis in the leg veins, an incidence of 1·61 per cent He also found an incidence of 1 2 per cent of puerperal thrombosis in 378,508 deliveries.

Murley[43] in a personal series of surgical cases very carefully examined by himself found a 9 per cent. incidence of thrombosis in 474 patients after operation. This appears high, but as he points out it was in a series of

mentation rate, reduced fibrinogen content, and alteration in the calcium and potassium content, but proof that these are important is lacking. Not only operation and injury but also parturition, infection and malignancy may result in blood changes, particularly increase in the platelet count. A constitutional factor has been considered important.[50] In experimental vitamin E deficiency there is a tendency for venous thrombosis to occur, and as a prophylactic measure the use of alpha-tocopherol has been suggested, calcium being given at the same time. Favourable results have been reported with these measures, but the figures quoted are not impressive, and the series of patients so treated have been small.[51, 52] Not all workers agree that alpha-tocopherol, or vitamin E, is in fact an antithrombin,[53] a basic assumption in the theory. We have had no experience of this therapy.

Little is known about the physics of laminar blood flow, but electrical charges of both the vessel and the constituents of the blood play a part[46] and any alteration in the cellular content of the blood is apt to disturb this delicate balance. Actual cellular increase, as in polycythaemia, and relative cellular increase, as in dehydration or haemorrhage, predispose to thrombosis in man.

Environmental temperature.—There is probably a climatic factor, the incidence of thrombosis being higher in winter and in cold climates than in summer and in warm climates,[50] but there may be other factors than temperature concerned such as the higher incidence of upper respiratory infections in cold damp weather, or alternatively the hibernal incidence may be due to the vasospastic effect of cold.

Other factors contributing to venous thrombosis.—Thromb[illegible] to hypercoagulability of the blood and perhaps sometimes to thrombosis. An incidence of 7 per cent. in patients under treatment with A.C.T.H. has been reported.[55]

PATHOLOGY

It is nowadays generally accepted, as a result of phlebographic studies,[45] autopsy studies,[46, 47] and, more recently, dissections of calf muscles[43] (Fig. 338), that post-operative or decubitus thrombosis starts in the small veins of the calf or foot in the vast majority of cases, and not as was previously thought in the iliofemoral or pelvic veins. Conner in 1904[48] anticipated a "white leg" in typhoid fever by several days or weeks by the detection of pain and tenderness in the calf muscle, although it is doubtful whether he appreciated the significance of the tenderness being due to thrombosis of the calf veins which was later to spread to and become adherent to the main vein of the limb with signs of venous obstruction.

In this case it might be assumed that lack of effective muscular activity after the tenotomy resulted in stasis in the calf veins with subsequent thrombosis. Other instances of thrombosis occurring after denervation of the calf muscles have been described.[44]

In heart disease, especially congestive heart failure, increased venous pressure accentuates the factor of stasis. White[45] found *thrombosis in the lower* limbs in 30 per cent. of all patients with congestive heart failure.

Age.—The older the patient, the more frequent is thrombosis In our series nearly ten times as many occurred after the age of forty than before this age, and three times as many after than before the age of fifty. Only three of sixty-nine fatal pulmonary embolisms occurred below the age of fifty. The increased incidence with age may be due to intimal defects occurring in the process of ageing Pulmonary embolism does, however, occur exceptionally in children and we have recently seen it in a child of seven after an operation for appendicitis with peritonitis. In infants and young children peripheral thrombosis is rare, but the visceral veins and the cerebral sinuses are occasionally the site of thrombosis with even more frequently serious results.

Malignant disease.—That there is an association between malignant disease and thrombosis has been known for many years, and peripheral thrombosis occurs as a complication of malignancy of abdominal organs and sometimes of the lung.

Sex.—In our series there were seventy-nine cases of thrombosis in women as against forty-five in men, and obstetric and gynaecological cases were excluded.

Obesity.—There are twice as many cases of thrombosis in patients over fourteen stones (196 lb.) than in those under that weight; it has been shown that after administration of a high cream diet to the experimental animal[46] there is a higher incidence of thrombosis, and that alimentary lipaemia increases the coagulability of the blood.[47] The lethargy often associated with obesity may be of importance too.

Intimal damage.—Most thromboses appear to originate in vessels in the calf muscles, and it may well be that this results from intimal damage,[48] possibly due to ischaemia, occurring as a result of the patient's calves resting on the bed or operating table.

Blood changes.—The significance of blood platelets in thrombosis was recognised by Bizzozero[49] who realised that damage to the vascular endothelium resulted in the adherence of platelets with subsequent thrombosis, the clot consisting of these structures and the white cells of the blood. Other changes in the blood which have been blamed for encouraging thrombosis include alterations in the albumen-globulin ratio, a raised erythrocyte sedi-

Savory[59] in 1866 first called attention to two types of venous thrombosis, one with few local signs or symptoms, but with a tendency to cause massive pulmonary emboli, and the other with pain, swelling and evidence of venous obstruction, but with little tendency to cause embolism. Since that time many writers[60] have re-emphasised this distinction, and the two varieties have been called phlebothrombosis and thrombophlebitis. These are descriptive terms and are, we believe, representative of different stages of the same pathological process, and not separate conditions as had been suggested.



FIG 339
Early thrombus in splenic artery Strands of homogeneous platelet material shown springing from the vessel wall and [illegible] ing between [illegible] ×65.

From a pathological point of view it is not easy to conceive of thrombosis,
which takes place in a column of blood in motion, occurring without some
alteration in the vein wall which has the effect of causing the blood platelets
to adhere to it It is well known—and was shown by Lister—that a column
of stagnant blood in a vessel, gently occluded at either end, will remain fluid
for a long time In the process of thrombus formation some alteration in
the physiological integrity of the vessel wall [illegible]

[illegible] hyaline bands running more or less at right angles [illegible] be seen under the microscope as and sometimes known as *Lines of Zahn* (Fig. 339). Simultaneously with the

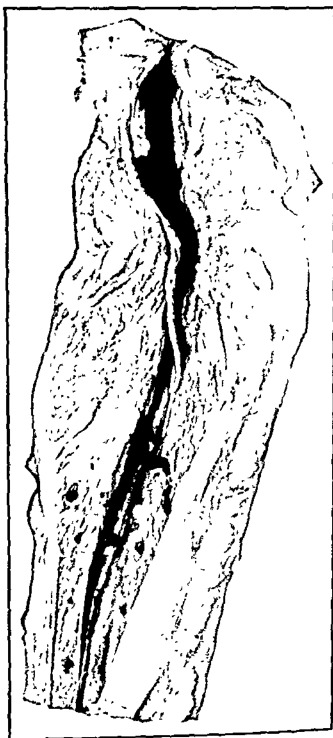


FIG. 338
A dissection of the calf muscles There is ante-mortem clot within the lumen of the veins.
(Morley—Annals Royal College of Surgeons, England)

polycythaemia. The red clot of a propagated thrombus may reach a length of one and a half feet and is the result of massive coagulation of a slowly moving column of blood. Where "phlebothrombosis" is present, therefore, there are no signs or symptoms of venous obstruction, and blood may still flow along the vein in which the clot is lying, but there is serious risk of its breaking off and being carried through the heart to lodge in the pulmonary circulation. If, however, the thrombus is so built up that obstruction of the vein occurs, propagation will cease at or about the point where a major incoming branch joins the affected vessel, and signs of venous obstruction will appear, such as swelling of the limb and varying degrees of cyanosis, and at this stage massive embolus is improbable. At the same time the vein reacts to the fixed thrombus in its lumen by an inflammation. This is now the stage of "thrombophlebitis". The amount of inflammatory reaction varies from a minimal response, to one involving all the coats of the vein wall and even extending *outside* to include the perivenous tissues; this may be so extensive as to involve the nearby artery, and possibly be a cause of the arterial spasm occasionally associated with thrombophlebitis. Alternatively a reflex kind of *vasospasm*, both arterial and venous, may result by way of the sympathetic nerves, and give rise in extreme cases to ischaemia or even gangrene (p. 658) as is probably so in those few cases when symptoms are relieved by paravertebral sympathetic block. It is inflammation of the vein which gives rise to *the pain, the tenderness* and the general reaction usually seen, these clinical effects being proportionate to the degree and extent of the inflammation.

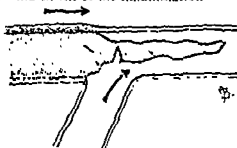


Fig. 340

Although in the stage of thrombophlebitis massive embolism is uncommon since the contained thrombus is fixed, smaller emboli may occasionally occur if a "tail" is formed proximally, and if this tail, unattached except at its base, extends past the orifice of a patent tributary vein and is broken off by the flow of blood (Fig. 340). This tail may frequently be seen floating free within the lumen of the saphenous vein at operation for spreading thrombophlebitis of the saphenous vein. When emboli occur during the stage of thrombophlebitis *they* are small and non-fatal, as the main part of the clot is firmly anchored by the inflammatory reaction of the vein wall, and it is only the tail which is not so attached.

Obstruction of the great vessels resulting from thrombophlebitis cripples the circulation in the limb, whether or not there is eventual recanalisation, for it permanently damages the valves *in the affected* vessels.

It has been claimed that thromb[illegible]
phleb[illegible] y distinct from
[illegible] the iliofemoral
[illegible] not, of course, deny the

building-up of these platelet masses there is a release of thromboplastic substances which cause the precipitation of threads of fibrin which fill the spaces between the lines of Zahn and may extend beyond the zone of platelet aggregation. A third important element in the thrombus is the mass of cells, red cells and leucocytes, which become caught up in the fibrin network. It must be understood that *the composition of a thrombus varies greatly according to proportions of its constituent elements.* A slowly-forming thrombus contains a predominance of platelets and is firmly anchored to the vessel wall. Such a thrombus will form in quickly-moving blood and thromboplastic substances play little part, since they are usually carried away by the blood stream. A thrombus with a high proportion of fibrin is likewise firm and pale and also moderately adherent, unlikely to be spontaneously detached. A rapidly-forming thrombus, such as may occur where there is a considerable element of stagnation in a column of blood into which thromboplastic substances can diffuse, will more closely resemble the clot *en masse* which forms in a test-tube outside the body. It is a fragile and not very adherent structure and is readily detached from the vessel wall.

As a thrombus grows older certain changes occur in it. Some of these may be of a chemical nature, such as the condensation and change in staining characters of the fibrin. Others are cellular, such as the autolysis and phagocytosis which tend to remove many of the cells included in the fibrin network. An especially important cellular phenomenon is the penetration of the thrombus and its overgrowth by endothelial cells which play a predominent part in the process of canalisation. Lastly, an invasion from the deeper layers of the vessel wall may lead to the process of organisation (*see* canalisation and organisation, p. 359). Where the wall of a vessel in which thrombosis is taking place is already the seat of pronounced inflammatory changes all the reactive events just mentioned will be accelerated, so that adhesion of the thrombus to the wall will be earlier and firmer.

The cause of spontaneous thrombosis *in vivo* is still a problem lacking complete solution and perhaps, in so complex a matter, it may fairly be said that no single and simple answer can ever be forthcoming As a result of trauma, haemorrhage, or increase in suprarenal activity there is a generally increased tendency to thrombosis. The platelet count rises, the clotting time shortens, and the amount of fibrinogen in the blood increases. If under these conditions a local factor, such as injury to the wall of a vein from pressure or other cause, or physical changes in the wall due to blood stagnation occur, increasing its adhesive effect on platelets, thrombosis may be set up. Other special factors, modifying the composition of the blood may sometimes intervene. Thus Quick[61] has noticed that in anaemia there is a tendency for retraction of this clot from the vein wall to be pronounced whereas in polycythaemia retraction is minimal, owing to the different cell volume in the two conditions, and it is interesting that pulmonary embolism is relatively more common and venous obstruction less common in anaemia than it is in

and for a few hours after operation have probably decreased the incidence of thrombosis[62] (p. 646). No attempt seems yet to have been made to correlate post-operative thrombosis with the metabolic (and adrenal) responses to operation.

CLINICAL FEATURES

The early diagnosis of thrombosis of the leg veins depends almost entirely on the vigilance of the patient's medical, nursing, and physiotherapy attendants. The clinician should constantly by example and by verbal repetition of the early evidence of the disease try to instil into his colleagues and also the nursing staff and physiotherapists a state of "thrombosis-consciousness" It can become a habit with the nursing staff to palpate the patient's calf and foot muscles for tenderness as the bed is being made, and with the physiotherapists on their post-operative visits.

In the stage of phlebothrombosis local reaction is minimal. At first, and indeed throughout the course of the illness there may be no evidence of venous obstruction The signs therefore have to be actively sought and consist of tenderness on palpation in the sole of the foot or in the calf muscles where it is generally but not always most evident on postero-anterior rather than lateral compression Dorsiflexion of the foot of the patient lying in bed causes pain in the calf muscles in a proportion of cases but this is not necessarily indicative of thrombosis and is often absent when thrombosis is present. This sign is often attributed to Homans but he has disclaimed it.

In about 75 per cent of cases there is pyrexia, and if this appears some time after operation and if there is no other apparent reason for it, thrombosis must be considered The temperature is in the region of 100° - 102° and may in some cases appear on the day of operation, but more often a few days after, and it may be the only sign of thrombosis. It is frequently accompanied by a moderate rise in pulse rate, and, it is said, by a feeling of uneasiness and anxiety. If in addition to pyrexia there is also some calf or foot tenderness, then the diagnosis is sufficiently sure to demand [illegible]

[illegible] thrombosis has been the cause.

Later, after an interval of days or sometimes a week or two, thrombosis may spread into the popliteal vein and if and when it has become adherent to the vein wall, evidence of venous obstruction will appear with oedema of the foot or leg associated with visible and prominent superficial veins. With the onset of an active inflammatory reaction of the vein wall there may be complaint of spontaneous pain, sometimes of great severity requiring morphia for its relief, but usually of lesser degree. Cramps, generally in the calf muscles and often nocturnal, are a frequent complaint. There is tenderness over the course of the veins which in the flexures of the limb may be palpable on examination Swelling becomes more marked the higher the thrombosis extends and in iliac vein thrombosis involves the whole thigh and

part that sepsis can play in the causation of thrombosis, there has been r bacteriological support for such a thesis, and it is entirely contrary to tl sequence of events in the majority of cases; as for example where the conditi follows operations remote from the affected area. Furthermore, it is n unusual for embolic incidents to precede the clinical picture of establish thrombophlebitis.

A female aged sixty-four was operated on for carcinoma of the right brea On the tenth post-operative day she developed pain in the right chest and X-r showed obliteration of the right costophrenic angle. There was a pyrexia of abo 100° F. but no sputum. On the sixteenth post-operative day the left leg from tl groin to the toes was grossly swollen with non-pitting oedema and cyanosis.

In this case the sequence suggests a sublethal pulmonary embolus from phlebothrombosis, the latter condition progressing to a massive iliofemor thrombophlebitis.

Phlebothrombosis occurs frequently in both legs yet one side only ma progress to thrombophlebitis. An embolism in such circumstances arises fro the leg the site of phlebothrombosis, that is, the leg with fewer and slight signs and symptoms.[50]

In post-operative cases the time of incidence of the thrombosis is variabl and is generally stated to be between the fifth and the twenty-fifth day with th highest incidence about the tenth day after operation. If the earliest evidenc is sought it will be found that the period is often considerably shorte Murley[43] noted that seven out of seventeen emboli occurred between the thir and sixth post-operative day, and thrombosis must have antedated thes incidents, and must have in fact originated very early in the post-operativ period.

We believe that many, if not most, cases of post-operative thrombosi start at or immediately after the operation. First, early rising, even on the da of or the day after operation does not necessarily prevent the occurrence o pulmonary embolism some days later It seems improbable, though not im possible, that thrombosis would begin in a leg at a time when it is bein actively exercised; it seems more probable that the thrombus starts during the day of operation or very shortly thereafter. Secondly, the pyrexia associatec with thrombosis often starts on the third to the sixth day after operation, bu it may also, and frequently does, start on the evening of the operation day and persist thereafter until the process resolves, or until adequate anticoagulan treatment is started, when a pyrexia from this cause falls dramatically. Thirdly, it is during and immediately after operation that the clotting mechanism might be expected to be most active; also it is frequently at this time that some degree of shock and dehydration is present, and the circulation is at its slowest, with the blood in the veins of the calves almost stagnant. That evidence of thrombosis is not forthcoming for some days is not surprising as we do not know how long it takes for clot to grow to such an extent as to become clinically evident. Finally, certain measures designed to prevent stasis during

state of the limb is irreversible, the patient is a cripple, major or minor, for life, and will require a permanent support in the nature of a bandage or a frequently renewed elastic stocking

Laboratory aids.—There are no laboratory tests at present available to predict the occurrence of thrombosis or even to prove its presence. Routine estimations of clotting times[63] and the presence of fibrinogen "B"[64] have been suggested as indicating a pre-thrombotic state, but they have not proved reliable[65] Changes in the platelet count, and alterations in platelet "stickiness" occur after operation but there is no point at which thrombocythaemia or platelet adhesiveness becomes conclusive proof of the presence or imminence of thrombosis.

VENOUS OBSTRUCTION OR THROMBOSIS AT SPECIAL SITES

Ilio-femoral veins.—In thrombophlebitis there is tenderness along the course of the femoral vein. Swelling of the limb is present tapering off gradually in the thigh, but often marked by rather a distinct upper margin. An aching heavy pain in the whole limb is usually present, but is not severe. Distension of superficial veins is sometimes seen, with a variable degree of cyanosis of the extremity If the thrombosis extends to involve the common iliac vein there is oedema over the buttock as well, but it seems that the thrombosis stops often at the junction of the hypogastric vein, no doubt because of the large flow of blood entering through this vessel. Symptoms of thrombosis of the pelvic veins which are sometimes encountered include tenesmus, a sense of fullness in the rectum, sciatic pain and frequency of micturition Urinary symptoms with a normal urine are suggestive of pelvic vein thrombosis[43] The circulation is maintained via the superficial veins of the abdominal wall and the gluteal and lumbar veins.

The inferior vena cava.—Obstruction of this vessel is usually the result of extension of thrombosis from an ilio-femoral thrombosis, although it may be due to compression by tumour, particularly of the para-aortic glands, or aneurysm It is associated with bilateral oedema of the legs, often the buttocks, and the lower part of the anterior abdominal wall. There is prominence of the superficial leg and abdominal veins, in which blood can be shown to be flowing upwards. In long standing cases the superficial abdominal veins may be markedly prominent and tortuous resembling those seen in advanced degrees of primary varicose veins of the leg. Symptoms are often remarkably slight, but there is always some bilateral chronic venous insufficiency of the legs (Figs. 342 to 344). [illegible]

The bladder drains by the periureteric veins to the renal veins. The uterus and ovaries also drain by these vessels, as well as by the iliolumbar and

sometimes the buttock. The more severe the phlebitis the more marked are the local signs and symptoms and marked tenderness is indicative of periphlebitis with involvement of perivenous tissues. Sometimes oedema after an operation or illness may be the only evidence of thrombosis.

Oedema associated with venous obstruction, as with most cases of thrombophlebitis, is of a soft pitting type, more marked in the foot and leg and gradually tapering off in the thigh. In some cases however, generally those associated with pain, and particularly with tenderness along the course of the vein, the swelling involves the whole thigh often with a sharply demarcated upper margin (Fig. 341). This is said to be due to lymphatic obstruction from involvement of the lymph vessels at the " bottle neck " in the groin by the perivenous inflammatory reaction. It has been suggested that this firm sharply demarcated swelling may be due to reflex arteriolar spasm with loss of the capillary pulsation that is important in the circulation of lymph, with consequent stasis in the tissues of the thigh, but if this was always the case it would be reasonable to suppose that it would resolve after paravertebral sympathetic block by local anaesthetic. Though very occasionally successful in relief of symptoms and swelling, the results of paravertebral block are usually disappointing, and we have never seen any beneficial effect in those cases in which the swelling does not pit on pressure and is sharply demarcated above. Furthermore, the swelling, though usually resolving with elevation and exercises in elevation does not always do so, because of, it is said, the inflammatory perivenous and perilymphatic effusion and obstruction of the lymph vessels at the root of the limb, although this has never been proved, but some degree of swelling may be permanent, although decreasing somewhat with postural treatment.



FIG. 341
Note the sharply demarcated upper margin of the swelling The thrombophlebitis followed an operation for hysterectomy, and was associated with much pain

Severe cyanosis is unusual except in limbs the seat of venous spasm, or massive venous thrombosis. Lesser degrees of cyanosis are however not uncommon, and sometimes, though rarely, there may be pallor and coldness of the extremity, the so-called phlegmasia alba dolens. The question of arterial and venous spasm in association with thrombophlebitis is discussed later.

Although the painful swollen limb may be the first evidence of a post-operative thrombosis, the more general awareness of the significance of an unexplained fever and calf tenderness together with the institution of proper anticoagulant treatment is resulting in such a limb being less commonly seen. It must be realised that once the main femoro-popliteal vein is obstructed the

state of the limb is irreversible, the patient is a cripple, major or minor, for life, and will require a permanent support in the nature of a bandage or a frequently renewed elastic stocking.

Laboratory aids.—There are no laboratory tests at present available to predict the occurrence of thrombosis or even to prove its presence. Routine estimations of clotting times[63] and the presence of fibrinogen "B"[64] have been suggested as indicating a pre-thrombotic state, but they have not proved reliable.[65] Changes in the platelet count, and alterations in platelet "stickiness" occur after operation but there is no point at which thrombocythaemia or platelet adhesiveness becomes conclusive proof of the presence or imminence of thrombosis

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ovarian veins to the lumber and left renal veins and inferior vena cava respectively.

The superior vena cava.—Obstruction of the superior vena cava is due to pressure from without by mediastinal tumour, primary or secondary,



FIG. 342
Inferior vena caval obstruction of long standing There is a bilateral post-phlebitic syndrome in the legs (Infra-red photograph)



FIG 343
Inferior vena caval obstruction Not infrequently there is little evidence of venous obstruction in the legs

aneurysm of the aorta or its branches, mediastinal infection, acute or chronic[66] and sometimes tuberculous, and, rarely to thrombophlebitis It may result from the strangulation of constrictive pericarditis.

Non-malignant tumours causing obstruction include lipoma,[67] fibroma, chondroma, myxoma, dermoid and other cysts,[68] and nerve tumours, neuro-

fibroma and ganglioneuroma.[67] Malignant tumours include primary neoplasms of the mediastinal glands, sarcoma and teratoma, and secondary tumours frequently from the bronchus, sometimes from other organs, oesophagus or breast. Tumours of the thymus and retro-sternal thyroid enlargements and enlargements of the mediastinal glands as in Hodgkin's disease and leukaemias may result in caval obstruction.



Fig 344
Inferior vena caval obstruction Infra-red photograph Infra-red photography is often helpful in diagnosis

When this vessel is obstructed there is swelling, often brawny, of both arms, with gross distension of the veins of the head and neck, cyanosis of the face and frequently proptosis. Dizziness, headache and sometimes mental confusion, increased on stooping, are often present, and the patient prefers sleeping in a half-sitting position to reduce congestion.

Pressure in the veins of the arms is increased, and may even reach 500 mm of water, whereas in the legs it is normal, a point which will distinguish those patients with similar symptoms in severe congestive heart failure Heart failure from diminished cardiac return may occur.

If the obstruction is above the level of the azygos vein, the orifice of this vessel being unaffected, there may be visible dilated veins over th... part of the sternum where a coll... the intercostal veins with the ... the azygos

vein is obliterated, then the circulation is maintained via the superficial thoracic and abdominal veins to the inferior vena cava. If similar symptoms of venous congestion are unilateral, then obstruction of the innominate vein of the affected side is to be suspected. If obstruction is acute in onset signs and symptoms are severe, but if it is chronic, compensation may be remarkable and symptoms comparatively slight (Fig. 345).

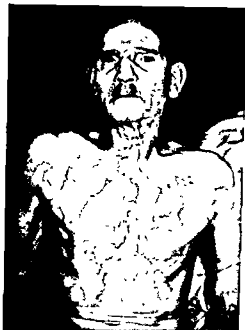


FIG. 345
Superior vena caval obstruction from mediastinal glands secondary to bronchial carcinoma.

Diagnosis of the cause of the obstruction *may be exceedingly difficult or impossible.* Venography will frequently help in demonstrating the site.

In non-malignant cases thoracotomy is to be considered. Many simple tumours and cysts can be removed with relief of symptoms, and a vein graft from the azygos vein to the intrapericardial portion of the superior vena cava, by-passing a thrombosed segment has been successful.[70] *Division of* a constricting pericardium will relieve *symptoms by relief of symptoms*; division of bands and adhesions surrounding the vessel has been reported.[71] Removal of an aneurysm may be possible. Deep X-ray therapy may be of value in some cases which result from inoperable malignant tumour within the chest.

THE POST-PHLEBITIC SYNDROME

This is the late result of thrombosis of the main leg veins. If the *thrombosis is originally detected and successfully treated* before it has spread to involve the popliteal vein, then permanent sequelae may be avoided, and if they occur, are slight. Thrombosis of one of the veins of the leg without extension to the popliteal vein does not result in significant venous obstruction for the collaterals are numerous, but when the popliteal vein has been affected then venous obstruction occurs and symptoms persist throughout life, becoming more severe and disabling with time.

Dilated superficial veins appear, acting as collateral *channels*, but these vessels rarely hypertrophy possibly because of the patient's age; rather do they *dilate, so that their valves become incompetent with still* further embarrassment of the venous return (Fig. 346). After an interval which may vary from one to ten years there is recanalisation of the deep veins.[72, 73] This does not lead to any relief of symptoms, for these veins have no valves, and the distal venous pressure increases with exercise instead of decreasing as it normally does[74]

As a result there is chronic venous congestion in the limb, a decreased oxygen and an increased carbon dioxide content in the blood, and nutritional changes apparent clinically in the skin and subcutaneous tissues of the lower part of the leg, usually above and occasionally below the malleoli Why the supramalleolar region is affected is not clear, but it may be due to the fact that the skin and subcutaneous tissues here are supplied by small tenuous arteries from above rather than by shorter branches taking origin from main vessels in the neighbourhood and reaching the subcutaneous tissues directly by perforating the deep fascia; as a result the pressure in these long narrow arterial channels is low and approximates to the pressure within the valveless veins, so that circulation is grossly impeded and nutrition of the tissues impaired More probably the views of Cockett and Jones[75] are correct. They have demonstrated the presence of a fairly constant communicating vein from the skin and subcutaneous tissues of the supramalleolar region on the inner side which joins the posterior tibial vein directly. Incompetence of the valve in this vein results in reflux with congestion and stasis at this, rather than at another site. This vein can be outlined by venography, and may also often be demonstrated at operation. The fact that ulcers always heal with recumbency and elevation, often necessarily prolonged, is contributory evidence that they are due to venous congestion



FIG. 346
Secondary varicose veins after deep venous thrombophlebitis There is moderate swelling of the ankle region.

At first the complaint is of swelling of the limb after standing, worse at the end of the day, but resolving after a night's rest. It affects the leg and ankle region and is limited by the restraining action of footwear, but as the condition progresses, swelling increases and the thigh may become affected. Infection, often from an eczematous patch, leads to fibrosis of the oedematous tissue, and resolution is then incomplete at nights. Lymphangitis and cellulitis occur not infrequently with heat, pain and swelling in the part but suppuration is rare. The inflammatory process often leads to contracture of the tissues with the production of a "waist" in the lower part of the leg and swelling above and below. Recurrent lymphangitis gives rise to increasing fibrosis of the subcutaneous tissues, with a tendency for the pitting oedema of a previous venous obstruction to become hard and resistant to pressure.

At first there is little but a feeling of heaviness but later, especially in the presence of inflammation, there is aching and pain, usually slight. Nocturnal cramps are often present.

Pigmentation occurs from the deposit of haemosiderin in the skin, and there is a tendency to eczema, preceded or accompanied by irritation. The

pigmentation, especially if associated with inflammation, may then proceed to ulceration (Fig. 347).



Fig. 347
Pigmentation, but little swelling, in a leg with deep thrombosis.

The eczema is usually of a scaly type, often with scattered subcuticular haemorrhages, but sometimes a weeping type is seen, which may be accompanied by severe *itching. The skin often becomes* sensitive to dressing materials. When ulceration of *the* legs occurs, it may do so either spontaneously or as the result of minor trauma. An abrasion may fail to heal, gradually enlarging to form an ulcer with weak, oedematous, dirty granulations and a papery thinness of the skin at the edges, or an indurated *pigmented area of skin may* break out into multiple ulcers, frequently after an attack of lymph*angitis or cellulitis. The ulcers tend to coalesce over* a large area and encircle the limb above the malleoli. They are quite typical and have a dirty, often purulent, base and a punched-out appearance which is due to oedema of the skin surrounding the ulcer and not to penetration of the deeper tissues by the ulcer. Pain is often not prominent, especially *in the larger ulcers. It is more* common in small ulcers on the medial aspect of the lower leg and behind and below the malleoli, and in these it may be severe, rendering the patient's existence intolerable. It may be that severe pain is due to involvement of the saphenous nerve, and it is noteworthy that division of this nerve at the level of the knee frequently gives relief. Ulcers which are painful are more often complications of primary varicose veins than of deep thrombosis and when primary varicose ulceration is present swelling is often absent (Figs. 348 and 349). The differential *diagnosis of leg ulcers is discussed elsewhere.*

Infection is rarely of serious moment, but a spreading cellulitis occasionally occurs in the subcutaneous tissues around an ulcer. A persistently infected ulcer may give rise to changes in the bone underlying it with subperiosteal new bone formation and patchy sclerosis and rarefaction, and even synostosis between tibia and fibula.

Carcinomatous change may occur in an ulcer of this kind provided it remains open over a long period of years, but it is uncommon, *and* chronic leg ulcers cannot be considered precancerous conditions. It may be that dermatitis rather than ulceration is the important predisposing factor[76, 77] Progressive growth of the ulcer in spite of proper supportive treatment, haemorrhage, hard prominent edges or a hard nodule in the groin are *suggestive of malignancy and demand biopsy* (Fig. 350). Radiotherapy has



FIG 348



FIG. 349

FIGS. 348 and 349. Primary varicose ulcers of leg The ulcer is small and painful There is minimal swelling and varicose veins are prominent.

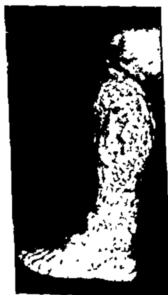


FIG. 350
Epitheliomatous change in a "varicose" ulcer of long standing
(By Courtesy of Mr H Dawtree Johnson)

pigmentation, especially if associated with inflammation, may then proceed to ulceration (Fig. 347).

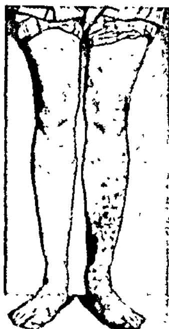


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PULMONARY EMBOLISM

The incidence of pulmonary embolism as a consequence of thrombosis of the leg veins is difficult to estimate, as minor embolism is not readily recognised, and thrombosis is not always detectable. The majority of large pulmonary emboli occur without any pre-existing evidence of thrombosis. Thus Zilliacus[80] reported that in 157 cases of fatal pulmonary emboli, thrombosis of the leg veins was not suspected in 124, and Barker *et al.*[81] found that in only 15 per cent. of 343 cases did clinical evidence of thrombophlebitis precede death, and in only 5 2 per cent. of fatal cases was previous thrombosis diagnosed As has been seen, large pulmonary emboli are likely to occur as a sequel of thrombosis only if there is a long tail of clot attached by its base to a segment of a vein wall, and floating freely in a stream of blood during the stage of phlebothrombosis, when symptoms are minimal or absent. In about 10 per cent. of autopsies after fatal pulmonary embolus, the origins of the embolus cannot be found,[82] but when a large clot is displaced, leaving only its base attached to a small vein in the calf, this is not surprising. Dissection of every vein in the leg muscles is impracticable, and so small an origin [illegible]

[illegible] complications occur they are not often attributed as they might sometimes properly be, to small non-lethal pulmonary emboli; in 1924 Lockhart-Mummery[83] suggested that non-fatal emboli may outnumber fatal by ten to one. Belt[84] described a special method of post-mortem examination of the pulmonary arterial tree and found that in three thousand unselected medical and surgical autopsies, pulmonary embolism was present in about one case in ten He emphasised the frequency of multiple small emboli, producing multiple small sterile infarcts which may together add up to a major embolism, obstructing more than half of the pulmonary circulation. He also found that embolism was about three times more common in medical than in surgical cases, which would be expected as the incidence of thrombosis in medical and surgical cases has a similar proportional incidence. Massive pulmonary emboli are rare in cases of thrombophlebitis of the deep veins of the leg when the clot is fixed within the lumen of the affected vein by the inflammatory reaction in the vein wall; it is extremely rare as a complication of chemical and varicose phlebitis, and it is practically unknown in thrombophlebitis migrans In suppurative phlebitis small infected emboli are common but massive embolism is not.

Of one hundred and fourteen patients with thrombo-embolism seen in the medical and surgical wards of Hammersmith Hospital, embolism occurred in 30 per cent. and was fatal in one-third of these. In many the embolism occurred before thrombosis of the leg veins was diagnosed. Jorpes (1946) reported that in the years before the active prevention and management of deep vein thrombosis the incidence of fatal pulmonary embolism was 18 per cent in patients with this condition, but with earlier diagnosis and suitable

been advised for patients in whom the diagnosis has been confirmed but this treatment often gives rise to large painful septic ulcers and Black[79] suggests that amputation should be done primarily. Inguinal glands should be excised



FIG. 351
Sarcomatous degeneration in a leg ulcer of twenty years standing, occurring in a male patient aged fifty-eight years.
(*British Journal of Cancer.*)



FIG. 352
Section of the ulcer depicted in Figure 351
(*British Journal of Cancer.*)

or treated by X-ray according to the general condition of the patient. Sarcoma has been reported occurring on the bases of leg ulcers and presents as a fungating mass in the centre of the ulcer[78, 79] (Figs. 351 and 352).

PULMONARY EMBOLISM

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Minor pulmonary emboli frequently pass undetected by the clinician, and when post-operative chest complications occur they are not often attributed as they might sometimes properly be, to small non-lethal pulmonary emboli; in 1924 Lockhart-Mummery[83] suggested that non-fatal emboli may outnumber fatal by ten to one. Belt[84] described a special method of post-mortem examination of the pulmonary arterial tree and found that in three thousand unselected medical and surgical autopsies, pulmonary embolism was present in about one case in ten. He emphasised the frequency of multiple small emboli, producing multiple small sterile infarcts which may together add up to a major embolism, obstructing more than half of the pulmonary circulation. He also found that embolism was about three times more common in medical than in surgical cases, which would be expected as the incidence of thrombosis in medical and surgical cases has a similar proportional incidence. Massive pulmonary emboli are rare in cases of thrombophlebitis of the deep veins of the leg when the clot is fixed within the lumen of the affected vein by the inflammatory reaction in the vein wall; it is extremely rare as a [illegible] of chemical and varicose [illegible]

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The effect of a pulmonary embolus varies according to its size and the state of the pulmonary circulation at the time. A large embolus, such as one which causes the fatal post-operative complication, is usually the result of the detachment of a propagated loose venous thrombus which, as has been said, commonly has its beginning in the small veins of the calf or foot. This cylinder of clot, which may be twelve inches or more in length, passes through the right side of the heart and becomes impacted as a coiled-up mass in the pulmonary arteries, at or just beyond their origin, effectively blocking the pulmonary circulation (Fig 353).



FIG 353

Post-operative [illegible] ve [illegible] the right [illegible] iology)

A small embolus may produce effects disproportionate to its size in the way already discussed If, however, the patient lives it will become permanently impacted in one of the smaller pulmonary arteries. In a normal lung with normal pulmonary and bronchial circulation no gross infarct is produced, the flow in the bronchial arteries sufficing to maintain the viability of the lung parenchyma. The impacted clot will be the seat of reactive changes in the pulmonary artery and [illegible]

treatment the incidence fell to under 2 *per cent. It may be that* this marked difference was the result, not only of treatment, but also of the more frequent diagnosis of the earliest cases of thrombosis as the result of the interest aroused by the introduction of the anticoagulants. In a patient *in whom the diagnosis of deep vein thrombosis has been made* and who is undergoing treatment by anticoagulants, pulmonary embolism is very rare, but if the patient is not so treated, his risk of embolism is about 10 per cent., and his risk of death about 1 per cent., death being often due to multiple small emboli, each in itself sublethal.

In a small general hospital admitting acute cases there were 3,663 medical, 11,365 surgical, and 7,237 obstetric admissions. Of these there were 65 deaths from pulmonary embolism, 39 occurring in medical cases, 25 after operations and 1 after childbirth. Fatal embolism thus occurred in 0·94 per cent. of medical and 0·22 per cent. of operation cases. Fatal pulmonary embolism appears to be considerably more common in medical than in surgical patients, and very rare in obstetric practice. In Bauer's series collected before anticoagulants were generally used, although 16·6 per cent. of patients with post-operative thrombosis succumbed from pulmonary embolism, only 3·6 per cent. with puerperal thrombosis died from this cause.

Once a minor pulmonary embolism has occurred, others are likely to follow. A non-fatal pulmonary embolus is followed in about one-third of cases by a further embolus, which is fatal in about a fifth of cases unless treatment by anticoagulants or proximal ligation has been carried out.

Emboli removed from the pulmonary arterial tree in fatal cases are massive and show no evidence of organisation. Therefore it may be assumed that it is only recent thrombosis which gives rise to embolism; intravenous thrombi which are adherent probably organise to some extent within twenty-four hours and if these were responsible, evidence of organisation would be found in the pulmonary clot. These massive and fatal pulmonary emboli frequently consist of the whole intravascular clot previously attached only by its base to a small calf vein.

On the other hand in " thrombophlebitis " emboli are smaller and arise from a tail of mobile clot freshly formed on the basis of the adherent clot. This is fractured, frequently by the flow of blood from a tributary vein Emboli so arising are rarely of sufficient size to be fatal in the first instance, but they may be followed by other multiple small embolisms with a fatal result. Recurrent embolism is, however, readily prevented by anticoagulant therapy

The actual cause of death in pulmonary embolism is not always clear. Death may occur when only one branch of the pulmonary artery is obstructed, and it has been suggested that it is then the result of a superadded arterial and bronchial spasm, but there is also a profound disturbance of cardiac action with right ventricular strain and failure, and it is probable that both pulmonary and cardiac effects contribute to the lethal outcome.

The effect of a pulmonary embolus varies according to its size and the state of the pulmonary circulation at the time. A large embolus, such as one which causes the fatal post-operative complication, is usually the result of the detachment of a propagated loose venous thrombus which, as has been said, commonly has its beginning in the small veins of the calf or foot. This cylinder of clot, which may be twelve inches or more in length, passes through the right side of the heart and becomes impacted as a coiled-up mass in the pulmonary arteries, at or just beyond their origin, effectively blocking the pulmonary circulation (Fig. 353).



FIG. 353

Post-operative pulmonary embolism A large mass of coiled clot extends from the right ventricle through the pulmonary artery, into the main branches of this vessel (Dible and Davie's Pathology)

A small embolus may produce effects disproportionate to its size in the way already discussed If, however, the patient lives it will become permanently impacted in one of the smaller pulmonary arteries. In a normal lung with normal pulmonary and bronchial circulation no gross infarct is produced, the flow in the bronchial arteries sufficing to maintain the viability of the lung parenchyma The impacted clot will be the seat of reactive changes in the pulmonary artery and both organisation and partial

canalisation occur with some restoration of the lumen of the pulmonary artery.[86] Harrison[87] has studied these effects in experiments in the rabbit and clearly shown that this is the fate of the embolus. It seems that at times there may be a certain amount of local lung damage and we have sometimes seen

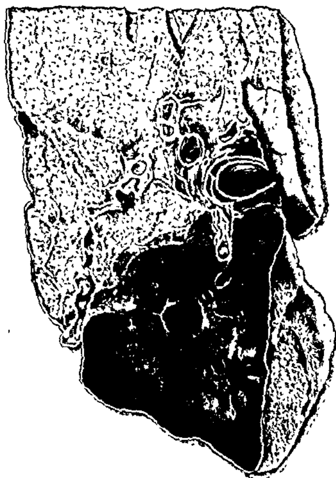


FIG. 354
Haemorrhagic infarct in the lung.
(*Dible and Davie's Pathology.*)

small organising infarcts in the lung, but these are rare and we do not know the conditions for their production. Multiple small pulmonary emboli are frequently to be found at post mortem especially where there has been a long agonal phase;[88] they do not appear to compromise the circulation to any serious extent.[84]

The familiar haemorrhagic infarct only occurs if there is some obstruction to the pulmonary veins which raises the tension in the capillaries and venules of the lung parenchyma, so that the force of the bronchial arteries does not suffice to keep the circulation going in the area supplied by the pulmonary

artery which has been obstructed by embolism. The best known example is mitral stenosis in which, in the stage of decompensation, haemorrhagic infarcts are notoriously common. Here the circulatory stagnation following on impaction of the embolus results in death of the alveolar walls and a general diffusion of blood into the lung parenchyma—an infarct in the literal sense—the whole of the affected area being converted into a hard blood-filled mass, usually roughly pyramidal in shape with the obstructed artery at its apex, and covered by pleura on which a fibrinous deposit quickly forms (Fig. 354).

Obstruction of the pulmonary arterial tree may occur not only from embolism, but also from primary pulmonary arterial thrombosis. It has been maintained[69] that pulmonary thrombosis is much more common than pulmonary embolism because the same blood changes are present in the pulmonary circulation as are present in the peripheral vein, and the pulmonary flow is normally sluggish and under a low pressure, especially when diaphragmatic movements are restricted as they often are after operations. Furthermore, a massive blood clot is often found filling accurately many branches of the artery. Belt[58] from a pathological viewpoint considers that primary pulmonary thrombosis is a rare phenomenon and he observed it in only ten out of 155 cases of haemorrhagic infarction of the lung seen in three thousand post-mortem examinations. In these ten cases he ascribed it to tumour invasion, tuberculous arteritis, the association of severe toxaemia or pre-existing pulmonary emboli

THE CLINICAL FEATURES OF PULMONARY EMBOLISM

A massive pulmonary embolus may obstruct both pulmonary arteries with instant death Sub-lethal embolism results in pain in the chest [illegible] noea, peripheral [illegible]

[illegible]

[illegible] chest wall overlying the infarcted segment is present The sputum, unless the [illegible]

[illegible]

[illegible] pain occurring in the post-operative period is often due to pulmonary embolism, and Cutler and Hunt[95] found that thirty-four out of sixty-three post-operative chest complications resulted from this

Pulmonary emboli do not always give rise to the typical clinical picture outlined above Any of the cardinal symptoms of pain, blood-stained sputum and consolidation of the lung may be present singly or in combination. Radiological evidence confirms the diagnosis in some cases, but the X-ray appearances are not very specific (see p. 256). Persistent [illegible]

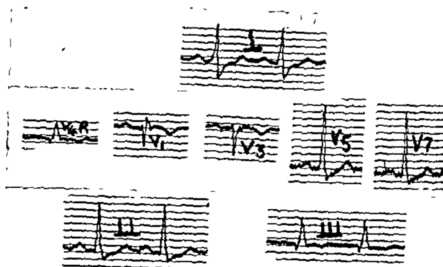


Fig. 355

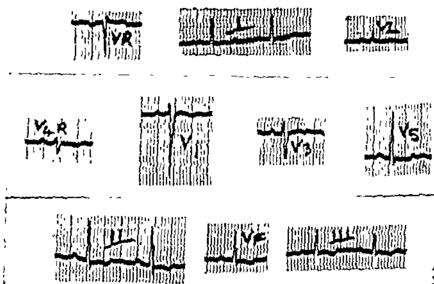


Fig. 356

Figs. 355, 356 and 357. Female patient, aged twenty-six years. She suffered substernal pain, circulatory collapse, raised jugular venous pressure, hypotension and triple rhythm occurring seven days after childbirth.

Fig 355. The cardiogram shows a prominent S wave in *lead I*, q wave in lead III; ST segment is iso-electric Chest leads show evidence of right ventricular dominance, dominant R wave in V_4R, and ST *in* V_1 T wave inversion in V_4R, V_1 and V_3. This is characteristic of acute right *ventricular* "strain" produced by pulmonary embolism.

Fig. 356. Same patient four days later, after clinical recovery Low *voltage T waves throughout, inverted in* V_4R, V_1, and V_3 indicate reduction in right ventricular "strain" The ST. depression is referable to digitalis

changes on X-ray may be the sole evidence of emboli. Blood-stained sputum and an opacity in the lung may simulate neoplasm; pleuritic pain, purulent sputum and basal opacity on X-ray may resemble a lobar pneumonia or massive collapse of a lobe, but the subsidence in pulmonary emboli and infarction is more rapid unless infection of the infarcted area results, and the response to anticoagulants is remarkable in embolic but not in pneumonic lesions

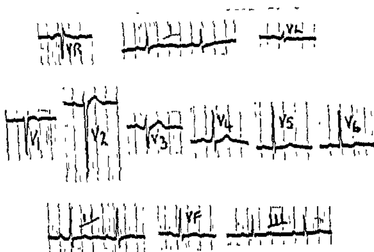


Fig. 357

Fig. 357 Same patient four days later The cardiogram is now almost within normal limits except for low voltage T waves in V_4 and V_5 and VL. There is no evidence of right ventricular "strain."
(Cardiogram kindly interpreted by Dr J F Goodwin.)

Larger pulmonary emboli by obstruction of the pulmonary circulation profoundly disturb the action of the heart, the more so if there is any myocardial or valvular disease There is lessened return of blood to the left heart, fall of blood pressure, pallor and a weak and rapid pulse. Gallop rhythm may supervene and then if the patient survives, venous pressure builds up, the peripheral veins distend, and cyanosis follows.

The electrocardiographic changes shortly after the onset of embolism indicate right ventricular strain and in the limb leads may resemble posterior myocardial infarction. There is a *deep S wave in lead I* with depression of *the S T* segment; a prominent Q wave in lead III with inversion of the T wave and elevation of the S T segment.[89] If chest leads are used pulmonary embolism can be distinguished from posterior myocardial infarction; in the former the T waves are inverted in *leads* V_1 to V_3 or V_4[90] (Figs. 355 to 357).

In those patients who recover from a large ... embolism it is not clear how ... It is possible that major ... and it may

be that a spasm of the pulmonary artery and its branches induced by the embolism, may relax.[91]

TREATMENT OF THROMBOSIS AND EMBOLISM

The treatment of these conditions is naturally divided into two parts—that directed towards the prevention of thrombosis and that directed to the established condition.

PREVENTION OF THROMBOSIS

Although important, stasis of the blood stream is not essential for the development of thrombosis. Thrombosis, as has been seen, often occurs in the ambulant patient. Measures directed towards the avoidance of stasis have affected the incidence of fatal pulmonary embolism but little,[92, 93, 94] although they have reduced the incidence of leg morbidity and, as a whole, thrombosis.

A man of thirty-five underwent operation for a right inguinal hernia From the day after operation he was actively ambulant, yet on the day of discharge eight days later, he died suddenly as a result of a massive pulmonary embolus

Most surgeons have experienced this kind of fatality. It is the early type of thrombosis, with the long fragile non-obstructing clot which originates so often, we believe, at the time of or a few hours after operation, that is the cause of these fatal emboli. The formation of this clot may well be complete before recovery from the anaesthetic.

There is nothing new in the idea of early ambulation as a prophylactic measure; it has been recommended for the last fifty years[95, 96] though more generally in recent times.[43, 94, 97] In spite of the fact that prevention of stasis affects the mortality from pulmonary embolus little, it is a measure to be actively encouraged as it is associated undoubtedly by a decrease in leg morbidity, in the incidence of detectable thrombosis[43] and perhaps in the incidence of minor pulmonary emboli.

Prolonged bed rest before operation should be avoided and for the avoidance of stasis and to maintain at its maximum rate the circulation in the limbs after operations the patient should be encouraged in deep breathing exercises which should be taught prior to operation. Avoidance of abdominal distension, the practice of bed exercises and early rising all help to maintain a rapid blood-flow in the limbs.

Holding the view, as we do, that a large number of surgical thromboses arise at the time of operation, or in the immediate post-operative period whilst the patient is still unconscious, Pearson[62] has devised the following régime.

1. During the operation the legs are supported by a sand bag, of sufficient size to relieve all pressure on the calves, placed under the tendo Achilles. At the end of the operation the patient's legs are held in elevation at an angle of 80° and firmly massaged from the ankles to the knees, and passive movements at the ankle and knee are carried out

2 The legs are maintained in 45° elevation during transport back to bed, and until the patient has recovered sufficiently to move the legs voluntarily. Great care is taken to ensure that blood in the veins is not allowed to become stagnant from the end of the operation until voluntary movement is possible (Fig. 358)

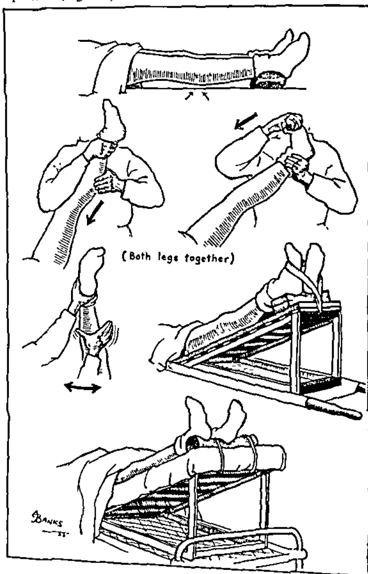


FIG. 358
(By courtesy of Mr A C. Pearson)

Pearson has personally observed each of 1,204 patients so treated during the last year during which time he has seen 5 with thrombosis whereas in the previous 1,531 patients there were 45 Though these figures are small, the

theory on which the system is based is sound, and the method is worthy of extended trial. One of its virtues is its simplicity.

In order to prevent stagnation of blood in the veins of the legs during confinement to bed for any reason the use of below-knee elastic stockings, exerting a pressure of 10 - 15 mm. mercury has been advocated.[98] It has been found that such a pressure increases considerably the rate of venous return from the legs, and it is suggested that the aneurysmal enlargements and saccular dilatations commonly present in the leg veins of older persons[99] are collapsed by it, a possible source of thrombosis being eliminated thereby. The use of these stockings is followed by a significant reduction of the incidence of pulmonary embolism and it appears that stockings applied to every patient medical, surgical and obstetric over twenty years admitted to hospital would reduce by half the expected incidence of fatal pulmonary embolism.[100] Such stockings should probably not be used for patients affected by ischaemic vascular disease of the legs, but there seems no other contraindication to their use. The use of elastic bandages as opposed to stockings is difficult and unreliable, and may indeed be dangerous owing to the possibility of excessively tight application.

Damage to the intima of veins must also be prevented. Pressure on the calf muscles with possible injury can be avoided during operations by supporting the weight of the legs on sandbags placed under the tendo Achillis and the legs can be protected by suitable pads when the patient is in the lithotomy position.

Alterations in the physico-chemical composition of the blood such as result from the anaemias, sepsis, diabetes and particularly dehydration and haemoconcentration are corrected as far as possible.

The prophylactic ligation of veins in suppurative thrombophlebitis was first advocated by Hunter in 1784 and has been practised sporadically in suppurative and non-suppurative thrombosis since that time During the past fifteen years there has been a considerable revival of interest in the procedure, more especially in thrombosis-prone patients, but widely conflicting results have been recorded. One important analysis of three separate five-year periods, during one of which 1929 ligations were performed including 871 for prophylactic purposes, showed that the incidence of fatal pulmonary embolism was virtually the same in all three periods[101] Furthermore routine prophylactic ligations would lead to a vast number of unnecessary operations, not without serious vascular effects in the limbs. It has been demonstrated that within one to eight years after ligation and division of the common femoral vein, serious sequelae appear in more than 75 per cent and after ligation of the superficial femoral vein similar complications occur in 10 per cent[102] We consider that there can rarely be a place for phrophylactic vein ligation at the time of the major operation.

The prophylactic use of anticoagulants, either heparin or dicoumarol has been wide, but there is no agreement on which drug, its dose or method of

administration will avert thrombosis without risk of post-operative haemorrhage. Intermittent intravenous administration of heparin has been widely used in Sweden and an extensive analysis in that country has been published to demonstrate its effectiveness.[80] In the same country, however, analysis of a series of 1,158 cases of thrombo-embolism in which heparin was used extensively showed that the mortality from pulmonary embolism was 13·9 per cent., whereas in the immediately preceding period during which heparin was used very little the mortality in 3,214 cases was 9·14 per cent.[103] De Bakey[104] quotes two series in which the coumarin drugs were used *prophylactically*; in one "a striking and significant reduction of thrombo-embolic complications" was claimed whereas in the other there was "fair but not striking evidence supported by statistical analysis" of the value of the therapy. These variations in reported results depend to a large extent on the diagnosis of thrombosis—sometimes very difficult, as is often the diagnosis of embolism—and reports on the prophylactic use of anticoagulant drugs are not convincing. The general practice in this country is to reserve the use of anticoagulants until such time as there is reason to suspect the presence of established thrombosis

Treatment of the Established Thrombosis

There are three available methods of treating established thrombosis and embolism.

1. Anticoagulant drugs.
2. Proximal vein ligation.
3. Paravertebral block of the sympathetic chain.

There are indications for each method of treatment, and it cannot be said that any one should be used to the exclusion of others.

1. Anticoagulant therapy.—As the prophylactic use of anticoagulants does not seem to have been significantly effective, it is the custom in Britain to reserve the use of these drugs for established cases of thrombosis. There are a certain number of patients who, during bed rest or after operation, develop a quiet symptomless thrombosis, and some of these die from massive pulmonary emboli. They offer no opportunity for the use of anticoagulants The earliest signs and symptoms of thrombosis—tenderness in the calf muscles, pyrexia and a raised pulse rate—are present only when there is sufficient reaction of a vein to a contained clot to provide some degree of adherence of the clot In such cases, although there may be a free tail of clot extending into the main vein of a limb, this will cease to grow and cause obstruction of that vein after anticoagulant therapy has been started for the anticoagulants prevent any new clot from forming. When diagnosis of thrombosis has been early, anticoagulant therapy prevents femoropopliteal venous thrombosis and the later development of a post-phlebitic syndrome. It may be that intravascular clot may even be dissolved to some extent by anticoagulants.[105]

In addition to their value in the prevention of the post-phlebitic syndrome anticoagulants prevent the addition of clot to established thrombophlebitis of the major veins. The small pulmonary emboli which occur in this type of case, and which tend to be recurrent and sometimes eventually fatal, are prevented. Emboli already lodged in the pulmonary circulation or thrombosis in these vessels is prevented from extending further and from transforming a minor to a major pulmonary occlusion. The beneficial effects of these drugs is reflected by the early resolution of the pyrexia and tachycardia usually associated with thrombosis and embolism, and this may sometimes occur within a few hours of the start of treatment. Pulmonary emboli may rarely occur when the patient is under anticoagulant treatment, but when this is so it is usually found that dosage has not been sufficient, or that it has been stopped before the patient becomes ambulant. It is essential that treatment is maintained for at least two days after the patient is allowed out of bed.

The details of anticoagulant therapy are given in Chapter XIX.

2. Proximal vein ligation.—Proximal vein ligation has been advised to prevent the escape of emboli from a limb known to be the seat of thrombosis.[106, 107, 108] Usually it is advised that the superficial femoral vein be first explored. If mobile clot is found in the vein, it may be removed by suction, and the vessel ligated. More usually, clot in this vein is tightly adherent with inflammation of the vein wall. This finding is invariable if the thrombotic limb is swollen. Higher ligation then becomes obligatory if it is to be done at all The external iliac vein is not suitable for ligation—its collaterals are not satisfactorily numerous—and in any case, if there is adherent clot in the common femoral vein, there is probably adherent clot in the external iliac too. The common iliac, which has a free anastomosis, must then be tied.

It is not always possible to be certain, however, from which side an embolus has taken origin Indeed if there is fixed thrombosis in the ilio-femoral trunk on one side the likelihood is that the embolus has arisen from loose clot on the other. It then is logical to ligate on the other side either the common iliac or the superficial femoral which will normally be found free of clot if there is no swelling of that limb.[50] Alternatively, the inferior vena cava may be ligated to trap emboli arising in either limb.[108, 109 110]

In our experience, as in that of other authors,[111] proximal vein ligation is nearly always followed by swelling of the limb whose vein is tied, although the incidence of this is distinctly less when the superficial rather than the common femoral vein is ligated. It is difficult to decide whether this is an effect of ligation, for swelling is inevitable once thrombosis has spread above the popliteal trunk. It is unprofitable to speculate on the proportion of blame attached to the ligation, and the proportion attached to the thrombosis for which the ligation is done. A more serious sequel of main vein ligation, phlegmasia caerulea dolens, is discussed elsewhere (*see* p. 658).

The operation of ligature is thus not free from its own dangers. Informed anticoagulant therapy reduces the occasions for vein ligation to a very few.

INDICATIONS FOR PROXIMAL VEIN LIGATION.

(a) *Septic thrombophlebitis with recurrent septic emboli, such as occurs particularly in lateral sinus thrombosis secondary to mastoid infection.*—The internal jugular vein is ligated.

(b) *Repeated pulmonary embolism which is not controlled by any other means.*—Patients under anticoagulants may continue to sustain pulmonary emboli and in these a timely proximal ligation may save life.

A male aged sixty-three, was admitted to hospital with pleuritic pain and haemoptysis. On examination he was found to have a tender calf muscle and minimal swelling of the left leg. Anticoagulants were given, but two further embolic incidents occurred during the two succeeding days. The left common iliac vein was ligated, as on exploration the common femoral vein was full of clot. No further emboli occurred but there remained swelling of the left leg and some cyanosis which were treated and controlled by compression bandages Four months later the patient presented again having noticed swelling of the right leg with calf tenderness. In view of the history of the thrombosis in the left leg, an immediate ligation of the right common iliac vein was performed. Convalescence was uneventful, but compression bandages on both legs were required and these will have to be worn permanently.

It is difficult to know whether the original emboli in this case arose from the limb that was first affected by overt thrombosis, or from an initially silent mobile clot in the opposite limb, which swelled later, but the cessation of embolism after the first ligation was dramatic.

(c) In certain conditions, for example *in jaundice or in the presence of severe renal dysfunction*, anticoagulants may be contraindicated, and it may be that on occasions *proper laboratory control* of patients under anticoagulants is not available, in such cases, in the presence of manifest thrombosis or embolism, proximal vein ligation may be considered.

3. Paravertebral sympathetic block with local anaesthesia.—The more often phlebothrombosis is recognised and properly treated, the less often will the stage of thrombophlebitis ensue Sometimes the swollen limb is cold and painful, sometimes pale and sometimes cyanosed, and then there appears to be a factor of vasospasm present. A paravertebral injection into the lumbar chain at the level of the second and third sympathetic ganglia then may occasionally be followed almost immediately by diminution of pain and swelling and by disappearance of pallor or cyanosis. Even though a dramatic relief is obtained only occasionally, paravertebral block should be tried if the limb is painful, swollen and really cool.[43, 119, 60] Paravertebral sympathetic block is dangerous in a patient under anticoagulant therapy, although some deny that there is any risk. The injection in such circumstances has on occasions produced an alarming and dangerous retroperitoneal h

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Support must be continued until the circulation has adjusted itself to the degree of venous obstruction which has occurred. In some less extensive degrees of thrombosis the tendency to swell may disappear after three months to two years, and support may be abandoned, but more usually, and probably always if the ilio-femoral vein has been obstructed, swelling will occur on standing, and support of the limb may be demanded permanently. As long as support is adequate complications in the leg will be avoided, but only too frequently is the post thrombotic limb neglected by the patient or even the physician with the later onset of all the symptoms of chronic venous insufficiency.

TREATMENT OF PULMONARY EMBOLISM.—Patients suffering from small pulmonary emboli are treated by anticoagulants, when the temperature and increased pulse rate so often present rapidly resolve. Pain is suitably controlled. Antibiotics are given for many post-operative bronchopneumonias probably start as multiple embolisms, and when clinical signs disappear, the patient is allowed out of bed Anticoagulants are continued for a few more days.

When larger pulmonary emboli have occurred the patient is often in a condition indistinguishable from that of extreme shock, and in addition to anticoagulants, measures to combat this must be taken. Warmth, relief of pain and continuous oxygen therapy are important, but intravenous fluids should be avoided so as not to overload the right heart Papaverine 30 mg ($\frac{1}{2}$ grain) and atropin sulphate 0 6 mg. ($\frac{1}{100}$ grain) are useful antispasmodics. After recovery from the acute stage, pleural effusion, fibrosis, infection of the lung and lung abscess may complicate pulmonary infarction, though their incidence is lessened by the use of antibiotics. There is no place for Trendelenburg's operation of pulmonary embolectomy; it is never possible, until the moment of death, to be certain whether a pulmonary embolism will be fatal or not, and more non-fatal embolisms are likely to be rendered fatal, than fatalities prevented in the hopeless ones.



FIG 360

Section of a vein wall and a valve flap. This shows the delicate valve flap rendered useless by an organised clot situated between it and the wall of the vein. The vein wall elsewhere shows no sign of phlebitis. A—valve flap B—vein wall.

TREATMENT OF THE ESTABLISHED POST-PHLEBITIC SYNDROME.—Many patients are seen for the first time with the post-phlebitic syndrome of swelling, induration, eczema and ulceration fully established. The original thrombosis which occurred, often many years previously, is forgotten or has passed unnoticed, and indeed it is doubtful whether the syndrome is always a sequel of thrombosis; proof of thrombosis is often entirely lacking (Fig 360). Many of these ulcerated limbs are the site of infection; this is not commonly of any significant degree, but if the skin in the region of the ulcer is hot, tender,

TREATMENT OF A LIMB THE SITE OF DEEP VENOUS THROMBOSIS—A patient with recent thrombosis of the deep veins of the leg should be rested in bed with the foot of the bed raised on 9-inch blocks to encourage venous return and to minimise swelling. When anticoagulant treatment has been started, though no attempt is made to reduce the freedom of the limb in bed, active exercises are not encouraged for three days. After this time the clot can be presumed to be firmly fixed within the lumen of the vein, and exercises in elevation can be prescribed, provided they do not cause pain or distress—the vein wall and perivenous tissues are often in a state of acute inflammation. The

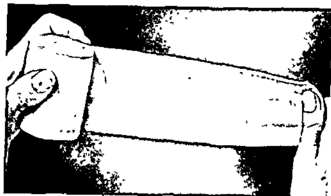


FIG. 359
This bandage, stretching longitudinally but not transversely, is of such an elasticity that when applied at full stretch the tension is correct.
(By Courtesy of Messrs John Bell & Croydon, Ltd.)

affected limb is kept warm to encourage vasodilation, and cold packs, so often advised, are to be avoided, resulting as they do in local vasoconstriction and slowing of the circulation. The patient is allowed out of bed when the pulse and temperature have been normal for two or three days, and when pain has gone. Any tendency to swelling must be controlled by the use of elastic bandages as soon as the patient becomes ambulant. It is absolutely essential that anticoagulants be continued for three or four days after the patient gets up, as this is a time when pulmonary emboli may occur.

The care of the limb following the acute phase is often neglected. Any *swelling of the leg must be controlled* by adequate supportive measures as long as there is any tendency for it to occur. As eczema, induration and *ulceration do not affect the lower limb above the knee*, although swelling is not necessarily so confined, support below the knee is generally all that is needed but if gross and disabling swelling of the thigh is present a full length stocking with a suspender support will be necessary. Elastic stockings are not always sufficient as after a few weeks they lose their elasticity, and constant replacement is a great expense. The use of elastic web one way stretch bandages (Fig. 359) applied before rising in the mornings, and worn until the patient is in bed at night is preferable, although for dress wear, stockings can be allowed.

the effects of ligation have in general been disappointing. There is some reason to suppose that pain of a bursting nature, an uncommon type of pain which persists in spite of adequate support and after healing of an ulcer, is relieved by main vein ligation[116, 117, 118] but venous pressure recordings have shown that after this procedure stasis is actually increased.[74] It may be that in the rare cases of iliofemoral thrombosis without distal extension there is a place for main vein ligation, but such cases must be very unusual. Cockett and Jones[75] consider that most ulcers originate over an incompetent perforating vein and advise ligation of this vein, and they record good results after this operation. It must be remembered that wounds in this area, particularly when malnutrition of the skin or ulceration is present, are often very troublesome and slow to heal We have recently seen a female patient who, after this operation for ulcer, developed tetanus and died. The surgical treatment of incompetent superficial veins complicating the post-phlebitic syndrome has been advised. If adequate support of a limb with chronic venous obstruction is essential, then there is nothing to be gained by treatment of the superficial veins, quite apart from the fact that further thrombosis is frequent when operations are performed on patients who have suffered previous venous thrombosis. Surgical treatment of secondary varicose veins can, however, be considered when swelling of the leg is minimal, when nutrition of the ulcer-bearing region is unimpaired, and when the superficial veins are found to be grossly incompetent

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indurated and swollen, the limb is rested in elevation and antibiotics are given parenterally. They should not be applied locally, especially penicillin, as they are irritant to an already sensitive skin and frequently aggravate its condition.[113]

Sir Benjamin Brodie in 1846 first noted the importance of adequate firm support in the treatment of post-phlebitic ulceration of the leg, to the exclusion of local ointments and dressings, and support still remains the mainstay of treatment, whether ulceration has occurred or not (Fig. 361) (*see* chapter on Leg Ulcers).



FIG 361
A one-way stretch bandage applied. If there is an ulcer in the concavity between the tendo Achillis and the tibia, or fibula, pressure is increased by the insertion of a felt pad over the ulcer



FIG. 362
Retrograde phlebogram The dye was injected into the femoral vein at the groin.

Lumbar sympathectomy has been claimed to cure the post phlebitic syndrome.[114] We have tried this in a number of cases, but unless the legs are bandaged, the ulcers, healed often by a period of rest following the operation, recur. It has occasional indications in a moist cold extremity, particularly one with severe dermatophytosis, which is inhibited by the dryness of the sympathectomised limb. Bauer[42] considered that the post-phlebitic syndrome results from recanalisation of a previously thrombosed main leg vein. Such a vessel he considered to be a rigid tube without valves, through which blood flows in the reverse direction. Retrograde flow can indeed be demonstrated by retrograde phlebography (Fig. 362), but controls are difficult to obtain, and it has not been finally decided what degree of retrograde flow can be considered abnormal.

Bauer[42] considered that ligation or resection of the popliteal vein would prevent the reflux and he has recorded remarkable results following this, as also have other authors after ligation of the superficial femoral vein,[115] but

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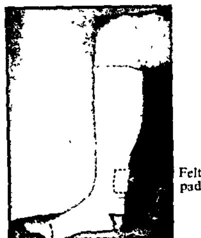


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a widespread venous thrombosis However this cannot be the case in that majority of patients who recover their circulation, sometimes rather suddenly.

When an isolated segment of vein is the site of thrombophlebitis there is accompanying venospasm extending beyond the affected vein, and this spasm can be relieved by anaesthesia of the vein wall or by paravertebral sympathetic block[12] The association of arterial spasm and thrombophlebitis has long been

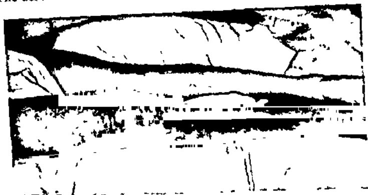


FIG. 363

Phlegmasia caerulea dolens in a female patient of twenty-eight years The onset was dramatically sudden and it subsequently subsided with a minor residual post-phlebitic syndrome

recognised,[13, 14] and severe temporary ischaemia of the forearm and hand after an infusion into the superficial veins at the bend of the elbow has been described.[15] Thus, at any rate in those patients who recover their circulation, partial venous occlusion by thrombosis may be rendered complete by spasm of the remaining veins of the limb, or there may be such a degree of arterial spasm that ischaemia is critical It is these two factors, varying in degree, which give rise to the different clinical varieties

The condition may be of medico-legal importance, for gangrene following operations for varicose veins does not necessarily mean that the main artery or even the main vein has been tied.

The treatment consists of anticoagulant therapy, measures to combat the initial shock—transfusions and infusions may have to be rapid and massive—elevation of the limb, and active exercises in elevation if the patient is fit. If the condition follows application of a ligature to a main vein, this should probably be removed[5] Sympathetic tone should be released by priscol, reflex heating and the induction of deep sleep. Operative or paravertebral sympathectomy should not be done on a patient undergoing anticoagulant therapy. In the event of major or minor gangrene, removal of tissue should be restricted to the dead part, as the circulation in the adjacent parts will have recovered completely by the time the need for ablation of dead tissue arises.

We have seen six examples of the disease, two in males aged sixty-three and sixty-seven, and four in females aged twenty-five, thirty, thirty-two and

CHAPTER XXI

MISCELLANEOUS DISEASES OF VEINS

PHLEGMASIA CAERULEA DOLENS

THIS condition variously known as gangrenous thrombophlebitis,[1] pseudo-embolic phlebitis, and blue phlebitis,[2] has attracted considerable attention recently, and the descriptive title, phlegmasia caerulea dolens, is now accepted.[3 4] As a result of venous obstruction, generally by thrombophlebitis, occasionally by ligature,[5] there is such interference with the circulation of the limb that its life is threatened and in fact gangrene results in about half the cases. Pulmonary embolism is common.

The lower limb is usually affected, but the condition has been reported in the upper limb.[6] It occurs in either sex, generally following thrombophlebitis occurring spontaneously or after operation, or in the puerperium, or as a result of pressure or invasion of a vein by neoplasm, or in association with blood diseases, especially polycythaemia vera.

Clinically, the onset is of dramatic suddenness with severe pain, gross swelling and cyanosis of varying degree which may sometimes be intense. Shock, due to loss of fluid into the swollen limb is often severe, and may be fatal. Arterial pulsation may not be detectable distally, and the limb soon cools to the temperature of its surroundings, so that the appearance may resemble embolism, a fact which has led to exploration of the femoral artery on a number of occasions.[7 8 9 10] Gangrene of any degree from a superficial necrosis to massive death of tissue may ensue, demanding a major amputation and this has been fatal in 25 per cent of recorded cases On the other hand the condition may slowly resolve, but resolution may be as sudden as the onset with complete recovery of the circulation without death of tissue, and a post-phlebitic leg may be the sole sequel (Fig. 363).

There are two main varieties of the condition, one with swelling and cyanosis, and one with arterial symptoms predominating, but usually the types are mixed, when both arterial and venous occlusion are suggested.

The cause is obscure Examination and dissection of limbs amputated for gangrene has revealed no evidence of arterial obstruction and although sometimes there appears to be a massive thrombosis of the main veins of the limb this is by no means always so. In one of our patients there was obstruction by thrombophlebitis of the internal saphenous vein only, which had followed an intravenous infusion of glucose saline. It has been shown experimentally that gangrene of an organ from venous obstruction occurs only when every vein draining that organ is ligated,[11] and it may be that some cases of phlegmasia caerulea dolens which proceed to massive gangrene result from

ficial veins of the leg with sometimes swelling of the whole limb. The pain may be severe enough to confine the patient to bed, and, though it is relieved by recumbency and elevation, it tends to recur on resumption of active use of the limb There are occasionally associated gastrointestinal disturbances, lower abdominal pain, headaches, and a minimal pyrexia. In the series reported by Pearson, nineteen out of twenty-two occurred during the same period in the nurses' home of a hospital, but epidemiological studies afforded no positive information Physical examination showed moderate swelling of the affected limb with marked tenderness over a palpable cord-like segment of the vein involved Biopsy of an excised segment revealed no thrombosis or obstruction but a thickened vein wall, and sometimes inflammatory changes in the vasa vasorum with leucocyte thrombi within their lumina. Blood examination and bacteriological studies showed no significant features. Pearson's description of the microscopical findings suggests an inflammatory reaction in some cases.

We have seen three patients with this syndrome, but in none was there any history of a similar condition in members of the same family or in associates

A married woman, aged thirty-two, reported with a history of a feeling of tightness, pain and swelling of the right leg and thigh. Two and a half months previously, whilst putting on her stockings, she had noticed a sudden tense feeling in the left thigh At first this eased off after resting, but on walking reappeared, often accompanied by a feeling of dizziness The symptoms persisted and [illegible] to [illegible] was [illegible] On [illegible] swollen, measuring 1″ more in the thigh and ¾″ more in the leg The left saphenous vein throughout its course from the groin to the foot was palpable and markedly tender. There was a minimal degree of erythrocyanosis and a history of chilblains affecting the backs of the calves; there was no cyanosis of the feet, and no varicosities of the legs. All pulses were full and palpable, the skin and subcutaneous tissues were healthy and there was no apparent difference in temperature in the two limbs.

Examination of the blood was negative, and the E.S.R., urine analysis and chest X-ray were normal.

A portion of the internal saphenous vein, half-way between the knee and groin, was excised, and section of this showed marked musculo-elastic thickening of the vessel's wall and of its valves: even if allowance were made for the possible effect of extreme spasm this degree of change appeared pathological (Fig. 3[illegible]).

A left paravertebral [illegible] ary relief of pain, and [illegible] complete relief of pa[illegible] saphenous vein was then stripped, unfortunately incompletely, but the patient was discharged from hospital one week later with relief of symptoms

Nine months later she reported again There was no tenderness and the swelling had almost gone, the left calf measuring ⅜″ more in circumference than the right, but she was still complaining of some pain in the left thigh Two years after operation there was no pain, and the swelling had disappeared.

fifty-seven. One occurred after ligature of the common iliac vein for recurrent pulmonary embolism, two after operations, one complicating thrombophlebitis of pregnancy, one complicating polycythaemia vera, and one occurring idiopathically. One patient died on the second day with gangrene developing at the level of the lower third of the thigh, one suffered a below-knee amputation for gangrene, and one developed a gangrenous ulcer which later separated and healed over the dorsum of the foot. The remaining patients recovered with residual post-phlebitic syndromes of varying degree. One patient suffered a minor pulmonary embolism.

MONDOR'S DISEASE

(String phlebitis of the chest wall: Phlébite en cordon: Sclerosing periangiitis of the lateral thoracic wall.)

Although occasional cases had been described previously[16, 17] Mondor's description in 1936[18] of this variety of phlebitis involving the chest wall has resulted in the eponymous title for the condition.

The disease consists of a phlebitis and periphlebitis of one of the veins of the chest wall particularly a vein below the nipple, extending from the anterior axillary fold towards the epigastrium. Other veins may rarely be affected on the chest and abdominal wall. At first painful and tender, and sometimes associated with a mild pyrexia, it is later felt as a firm subcutaneous cord attached to the skin, which slowly resolves and after six to eight weeks disappears. Sometimes it may branch, or even form a plexiform subcutaneous mass. Suppuration never occurs.

The essential lesion appears to be a phlebitis and periphlebitis of a superficial vein of the chest wall, and a similar inflammation of a nearby lymphatic vessel has been reported.[19] It may be difficult to decide on microscopical examination of a segment removed by biopsy whether an artery or vein is the site of the lesion, and the use of the term " angiitis " rather than phlebitis has been suggested.[20] There is a striking degree of periangiitis in the cases examined, and it has been suggested that this perivascular inflammation is the primary lesion.[20]

The cause of the disease is unknown. Muscular strain,[16] a pre-existing influenza-like illness, carcinoma of the breast,[19] local infection[19] and trauma associated with tight strapping of a wound after operation[21] have all been suggested as possible causes.

No treatment is necessary for the condition as it is self limiting and resolves in the course of a few weeks.

PHLEBODYNIA

In 1953 Pearson[22] published twenty-two cases of a hitherto unrecognised condition consisting of pain and tenderness over the course of one of the super-

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Two other cases of apparently the same character occurred in middle-aged men.



Fig. 364
Vein from patient suffering from "phlebodynia"

PHLEBOSCLEROSIS

Sclerosis of the veins, or phlebosclerosis, is unusual and is not associated with atherosclerosis. It occurs in males between twenty and forty years of age, but is infrequently recognised as there are no associated symptoms. There is no fatty deposit in the vein wall, nor is there any calcification, and the condition is not associated with hypertension. It affects mainly the leg veins, superficial and deep, and the former may be felt as hard subcutaneous cords which may be mistaken for tendons.

Microscopical examination of the vein wall shows thickening with increase of connective tissue in the media, atrophy of muscle fibres and fibrosis of the intima, and as a result of these changes the lumen of the affected vessel is narrowed. There does not appear to be any particular tendency to thrombosis.

The nature of the condition is uncertain, and the cause unknown.[23] It has been considered that persistent venous hypertension may be a factor in the development of the sclerosis.[24]

P M

Although the course of the long saphenous vein is quite constant, the number and the position of its tributaries are variable and a number of detailed studies of the possible variations, particularly at the sapheno-femoral junction, have been made[6] (Fig. 365). A knowledge of these variations

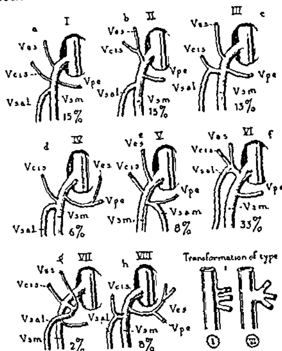


FIG. 365

Diagrams of saphenous tributary patterns. All shown as of right thigh Types (8) indicated by Roman numerals Percentage occurrence in 350 consecutive

trunk (VI), through lateral protrusion of area of convergence

(*Daseler, Anson Reimann Beaton—Surgery, Gynecology and Obstetrics*)

is valuable and indeed necessary for the success of the operation of high saphenous ligation The most consistent arrangement of the tributaries in the groin is that of three branches: the superficial circumflex iliac vein running downward parallel to Poupart's ligament from the anterior iliac spine, the superficial epigastric vein running downward from the anterior abdominal wall and the superficial external pudendal vein running laterally from the external genitalia. Not infrequently two of these tributaries unite to join the long saphenous vein by a common trunk The most commonly encoun-

CHAPTER XXII

VARICOSE VEINS

THE adjective "varicose" means dilated and by usage the term is restricted to dilatations of the subcutaneous veins of the legs but it is also applied to dilatations of the veins of the pampiniform plexus, of the haemorrhoidal veins and the veins of the lower oesophagus in portal hypertension. With the latter exceptions, the term "varicose veins," for all practical purposes, is limited to varicosities of the lower limbs since such a condition elsewhere in the body is relatively uncommon.

Varices of the superficial veins of the legs have been recognised and studied from the time of Hippocrates (460 - 375 B.C.) and the operative treatment was first mentioned between 155 - 86 B.C. Since these early observations the superficial varix has continued to perplex the medical profession and it may be said that even today the ideal treatment has not been discovered This is manifest by the return by many surgeons to treatment considered, tried and rejected many years ago. Of modern treatment it may be stated that the majority of patients can be cured or considerably improved by adequate surgery but there remains a recalcitrant minority of recurrent varicosities which defy even the most concerted attacks. These remain as a challenge to the vascular surgeon.

ANATOMY OF THE SAPHENOUS SYSTEM OF VEINS[10]

The saphenous system of veins is exclusively responsible for superficial varicosities in the lower limb. This system is made up of the long and the short saphenous veins, the former of which is the more susceptible to varicose disease although not infrequently both veins are involved in the same limb

The long saphenous vein, extending from the dorsum of the foot to the groin, is the longest vein in the human body. It begins by the union of the veins of the dorsal venous arch of the foot and passes upwards constantly lying immediately anterior to the medial malleolus at the ankle joint. Thence its oblique ascent follows the internal border of the tibia in close company with the saphenous nerve to reach a position just behind the medial condyles of the tibia and the femur From the knee the long saphenous vein passes upwards and outwards to the groin where it pierces the cribriform fascia of the fossa ovalis to join the femoral vein. The fossa ovalis lies approximately 2 cm. below and 3 cm. lateral to the pubic spine and it is a circular or oval aperture in the deep fascia of the leg. In its course up the leg the long saphenous vein lies in the subcutaneous tissues superficial to this deep fascia, supported only by the skin and superficial fascia.

this part of its course by the sural nerve. At first superficial to the deep fascia, it pierces the latter at the junction of the middle and upper thirds of the leg to lie between the two heads of the gastrocnemius muscle. Thus the short saphenous vein is supported not only by the deep fascia but also by the gastrocnemius muscle before it joins the popliteal vein in the popliteal fossa. This anatomical arrangement, and also its shorter course, are probably important factors in explaining its less frequent involvement by varicose change. Like the long saphenous vein, the short saphenous vein has numerous communications with the deep veins of the leg but these communications are seldom of the same practical importance as those of the long saphenous vein. In severe varicose veins the two saphenous systems may become almost one from the enlargement of numerous communications which in health are insignificant and relatively functionless.

Both the long and the short saphenous veins are plentifully supplied with bicuspid valves, the constancy and disposition of which are somewhat irregular. The most constant site of such valves is just below the junction of a tributary with the main saphenous vein. A similarly situated valve is found universally at the terminations of the long and short saphenous veins themselves with the femoral and popliteal veins respectively. Valves are found in the communicating veins between the superficial and deep venous systems, the function of which in health is to maintain directional flow of blood from the saphenous veins into the deep veins of the leg.

PHYSIOLOGY AND PATHOLOGY[10]

In the normal state blood flows from the legs towards the heart chiefly by the momentum given to the blood by the heart (vis a tergo) and by the pumping effect of the muscles, directly upon the deep veins and indirectly upon the superficial veins. Lesser factors are the respiratory action (vis a fronte) and the hydrostatic pressure, both of which may be operative against the return of blood to the heart at definite points in their cycles. The venous valves play a major rôle in maintaining directional blood flow towards the heart, particularly in the presence of muscular contractions, so that retrograde blood flow does not normally occur. Valve function is of particular importance with regard to the communicating veins between the deep and the superficial systems of veins. There is general agreement that normally the direction of blood flow is from the poorly supported saphenous veins to the muscularly clothed deep leg veins so well supported in their fascial compartments.

Under pathological conditions of the venous system of the legs in man alterations in the rate and the direction of blood flow occur and with these alterations there may be changes in the intralumenal pressures. When veins become varicose the rate of blood flow within them becomes less rapid and this is associated with an increase in the lateral pressure on the vein wall, even though the law that lateral pressure in a fluid stream is inversely pro-

tered additional branches are the medial and lateral superficial femoral veins which join the long saphenous after draining the medial and lateral aspects of the thigh. The above veins are situated normally superficial to the deep fascia of the thigh and they may become so enlarged as to become more prominent than the main saphenous trunk, whence the term "accessory" saphenous veins is applied. Occasionally such a vein, or the long saphenous vein itself, may perforate the deep fascia of the leg below the fossa ovalis and only lesser tributaries enter via the fossa ovalis.[9] If such a condition is not recognised the dilated tributaries joining the long saphenous vein may be mistaken for the sapheno-femoral junction with inevitable recurrence. A deep pudendal vein is frequently encountered joining the medial aspect of the sapheno-femoral junction deep to the fossa ovalis. The best approach to the antomy of the termination of the long saphenous vein in the groin is to assume that there is no normal arrangement so that a careful and complete exposure of the sapheno-femoral junction and meticulous dissection and division of all the tributaries encountered in that region becomes necessary in every instance.

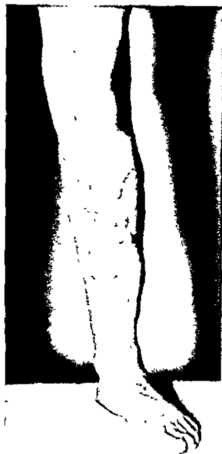


FIG. 366
Below-knee "blow out" with prominent anterior tibial varix

In the thigh and the leg the long saphenous vein has numerous communications with the deep veins and with the short saphenous vein. The most frequently enlarged communication between the long and the short saphenous veins is one which runs downward and laterally above the patella to reach the short saphenous before its termination. The most frequently encountered communications between the deep veins of the [illegible] just above

and below the knee (Fig. 366) T[illegible]

distal to the joint and the former a similar distance above it Although these are the most constant sites of "blow-outs," leaks from the deep to the superficial system of veins may occur at any point in the length of the long saphenous vein.

The short saphenous vein is formed by the junction of the lateral part of the dorsal venous arch of the foot with dorsal vein of the fifth toe. It passes below the lateral malleolus of the ankle joint and ascends along the outer edge of the tendo-achilles to reach the middle of the calf, accompanied in

this part of its course by the sural nerve. At first superficial to the deep fascia, it pierces the latter at the junction of the middle and upper thirds of the leg to lie between the two heads of the gastrocnemius muscle. Thus the short saphenous vein is supported not only by the deep fascia but also by the gastrocnemius muscle before it joins the popliteal vein in the popliteal fossa. This anatomical arrangement, and also its shorter course, are probably important factors in explaining its less frequent involvement by varicose change. Like the long saphenous vein, the short saphenous vein has numerous communications with the deep veins of the leg but these communications are seldom of the same practical importance as those of the long saphenous vein. In severe varicose veins the two saphenous systems may become almost one from the enlargement of numerous communications which in health are insignificant and relatively functionless.

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portional to the rate of flow does not hold absolutely for such slow-moving streams as dilated veins. Such a situation is conducive to progressive dilatation of the vein and the valves become incompetent. Two major abnormalities follow. First, blood may now pass from the deep to the superficial system of veins, in contrast to the normal situation, and so their burden is increased, their intralumenal pressure rises to abnormal heights and their varicosity becomes progressive. Secondly, retrograde blood flow or reflux occurs in response to posture, respiratory efforts and rises in intra-abdominal pressure. Even though such reversal of blood flow in the veins may be temporary, it is abnormal and if oft-repeated leads to progressive dilatation. The major cause of these altered circulatory dynamics is valvular deficiency, but whether the valvular deficiency is primary or secondary has not been established Nevertheless, the above circulatory alterations lead to stagnation of venous return in the superficial, namely the saphenous, veins.

The venous pressure in the long saphenous vein is normally the hydrostatic pressure between the level of measurement and the right atrium of the heart. At rest in the erect position the pressures in the normal vein and the varicose vein are similar, but with exercise the pressures show significant divergence. Normally the pressure in the superficial veins of the leg falls with exercise, for blood passes from them into the deep veins by virtue of the indirect pumping effect of the muscular contractions aided by the venous valves In varicose veins, especially where there are incompetent valves in the communicating channels, blood is forced back down the veins and from the deep to the superficial veins so that the pressure in the superficial veins becomes abnormally high. This is even more marked when the varicosities are secondary to deep venous insufficiency such as occurs in the recanalised stage of deep venous thrombophlebitis. There is also some evidence to suggest that at rest in the recumbent position the pressure within a varicose vein is higher than that within the normal vein, *i.e* it actually exceeds the hydrostatic pressure that would be expected. Be that as it may, it is abundantly clear that a varicose vein is subjected to a much greater daily strain than is the normal vein, and that once varicosity is established the deranged circulatory physiology favours progressive dilatation of the affected vein

The pathological changes that result from the abnormal circulatory state in varicose veins depend upon the degree and the duration of varicosity and the presence or absence of complications. The stagnation of blood flow and the increased intravenous pressure produce a number of morbid anatomical changes in the affected veins, the most frequent of which are elongation, tortuosity, localised dilatations or thickening of the vein walls and atrophy of the valves. The initial response of a vein to an increased intralumenal pressure is "arterialisation" or hypertrophy, a response in which all the elements of the vein wall participate. Although an increase in the elastic tissue and muscular hypertrophy occur, and may be prominent, the thickening of the vein wall is chiefly due to excessive fibrous connective tissue which

may be marked in the subendothelial layer. If previous thrombosis has occurred the hypertrophy is often considerable and evidence of recanalisation may be noted. Ultimately the effect of long-standing abnormal pressure and vascular stagnation with associated tissue anoxia is excessive dilatation and thinning of the vein walls, a change particularly prominent in the elderly and in those veins which lie immediately under atrophic skin with little support from the subcutaneous tissues. Such dilatations commence frequently at the site of an incompetent communicating vein and may be termed "blow-outs." This out-pouching of the vein wall is accompanied by a loss of elastic tissue and atrophy of the medial coat of the vessel, changes which lead to severe impairment of elasticity of the vein and so progressive dilatation. Associated incompetency, atrophy or complete disappearance of the valves is present, and this valvular destruction remains as an important pathological feature of varicose veins.

Apart from the above morbid anatomical changes, certain alterations of normal tissue environment are produced by the excessive venous pressure and circulatory stagnation. The abnormal venous pressure backs up into the venules and capillaries leading to deficiencies of tissue oxygenation and nutrition which are exaggerated by the increased capillary permeability and dilatation due to actual anoxia of the vascular endothelium. Excessive extraction of oxygen from the blood in varicose veins has been demonstrated[59] and that, with the abnormally high pressures, leads to oedema of the tissues and the passage of red blood cells through the damaged capillary walls into the tissues where they become haemolysed to produce the characteristic coppery discoloration of the skin. The deranged dynamics of the capillary bed circulation result in the skin and subcutaneous tissues becoming oedematous, anoxic and infiltrated with haemolysed blood so that their natural resistance to trauma and infection is lowered and the stage is set for the development of stasis dermatitis, lymphangitis and ulceration.

ETIOLOGY

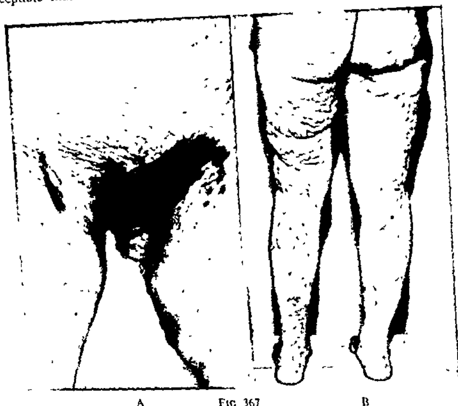
In the lower extremity varicosity of the long saphenous vein and its tributaries accounts for more than 90 per cent. of all varicose veins, the remainder occurring in the short saphenous system. Varicose veins may be **primary** or idiopathic, developing spontaneously in the absence of any demonstrable venous obstruction, or they may be **secondary** or compensatory, developing in the presence of proximal venous obstruction or deep venous insufficiency. Between 10 and 17 per cent. of the population are affected by varicose veins and women suffer about three times more frequently than men.[19] Although all ages may be affected the peak incidence is in the fourth decade of life and more than 75 per cent. of patients present after the age of thirty years.

portional to the rate of flow does not hold absolutely for such slow-moving streams as dilated veins. Such a situation is conducive to progressive dilatation of the vein and the valves become incompetent. Two major abnormalities follow. First, blood may now pass from the deep to the superficial system of veins, in contrast to the normal situation, and so their burden is increased, their intralumenal pressure rises to abnormal heights and their varicosity becomes progressive. Secondly, retrograde blood flow or reflux occurs in response to posture, respiratory efforts and rises in intra-abdominal pressure. Even though such reversal of blood flow in the veins may be temporary, it is abnormal and if oft-repeated leads to progressive dilatation. The major cause of these altered circulatory dynamics is valvular deficiency, but whether the valvular deficiency is primary or secondary has not been established Nevertheless, the above circulatory alterations lead to stagnation of venous return in the superficial, namely the saphenous, veins.

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too early in pregnancy to be explained by it For these a neat hydraulic theory proposes that the increased pelvic blood flow consequent upon pregnancy engorges the iliac veins sufficiently to interfere indirectly with venous return from the lower limbs (Figs 367A and B). The sex difference is probably an expression of the aggravating effects of pregnancy and motherhood in a susceptible individual. Increasing age is accompanied by deterioration of



A Fig 367 B

(A) Severe vulval varices associated with pregnancy (B) Superficial varices on posterior aspects of thighs in same patient and spider varices on the legs, incompetent long saphenous veins had been previously treated by high ligation

venous valves, and the skin and subcutaneous tissues become inelastic, thin and atrophic These changes are reflected in the fact that more than 75 per cent of all varicose veins arise after the age of thirty years

Occupation plays a definitely aggravating rôle particularly in individuals who stand for long periods without moving so that the prolonged effects of gravity are not opposed adequately by muscular activity A prime example of this has been the British housewife standing in queues, and other examples include dentists, ticket collectors, lift operators and waiters Nurses and policemen on the beat suffer relatively less in virtue of the muscular exercise associated with their occupations, a fact which is borne out by the relative rarity of varicose veins amongst athletes. Constricting bands around the legs or thighs

With regard to the etiology of the primary type of varicose veins there is great dispute, indeed the hereditary tendency is the only generally accepted factor, but whether the inherited weakness is located primarily in the vein wall or in the venous valves has not been established. At least 80 per cent. of patients presenting with varicose veins have a family history of varicosities, the pattern of inheritance being a simple dominant. Apart from inheritance, the rôle of which seems to be irrefutably established, there is only one other factor of undeniable importance and that is the erect stance. The significance of posture is exemplified by the great rarity of varicose veins in the upper extremity and the fact that they are unknown in quadrupeds. Although nearly all human beings are exposed to the erect posture a relatively small proportion appear to have inherited the tendency towards the formation of varices; in 10 to 17 per cent. of the population clinical varicose veins develop either spontaneously or with the added influence of secondary factors to be mentioned below.

The transmissable weakness in the structure of the veins probably lies chiefly in the walls of the veins and to a lesser extent in the valves. In the absence of such a hereditary weakness the superficial veins are able to withstand, without dilatation, increases of intravenous pressure associated with straining, coughing, pregnancy and the erect stance. When, however, structural weakness of the vein wall is present the vein tends to dilate just distal to the valve which soon becomes incompetent since its cusps no longer approximate. This leads to a greater strain being taken by the valve below so that each valve in turn becomes incompetent, atrophic and eventually destroyed. An interesting theory was advanced suggesting that the absence of valves in the major veins above the saphenous opening placed an abnormal strain on the saphenous valve which eventually gave way under this unrelieved hydrostatic pressure.[7] If this were true about 29 per cent. of people should have unilateral varicose veins and about 8 per cent. bilateral varices, for in 29 per cent proximal valves are absent on one side and in 8 per cent. on both sides Recent studies on the distribution of valves in the deep veins with relation to the presence of superficial varicose veins have failed to correlate the absence of proximal valves with the occurrence of saphenous varicosity[3, 16] Numerous precipitating factors have been put forward as causes of iodopathic varicose veins but it seems improbable that any one of them alone would cause varicosity in the absence of a fundamental structural weakness of the affected vein. The more important secondary factors are age, occupation, pregnancy, sex and endocrine changes. The last two of these are interlinked since endocrine disturbances are most frequent in the female at times of pregnancy, menstruation and the menopause but on the whole an endocrine hypothesis bears little scrutiny. The effects of pregnancy appear to be more definite. A purely pressure effect of the enlarged uterus on the pelvic veins leading to back pressure in the veins of the extremities would appear to be the simplest explanation but in a certain proportion of cases varicose veins arise

varicosities of the superficial veins are considered to be primary or secondary, all patients who develop varicose veins have the same type of hereditary weakness of venous architecture. This probability is reinforced by the observation that iliofemoral thrombophlebitis is more likely to occur in an individual with a family history of varicose veins than in one without such an influence and it is generally agreed that, apart from pregnancy, the commonest cause of secondary varicose veins is antecedent deep venous thrombophlebitis.

CLINICAL FEATURES

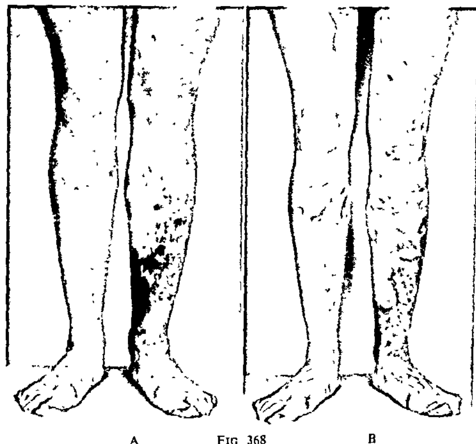
The features of varicose veins are so common that the patient usually applies the term "varicose" to the dilated leg veins when presenting for examination. A careful history is taken to ascertain whether or not there is evidence of antecedent deep venous thrombophlebitis, pelvic tumour or some other associated condition which might influence the course of treatment. The age of the patient, the presence of anaemia, leukemia, cardiac or renal disorders or splenomegaly may be associated with varicose veins which are purely incidental Such constitutional conditions may be detected by a general history and physical examination.

Unless the veins are secondary to deep venous insufficiency they may be extensive and yet quite symptomless. Generally speaking, the complaints from varicose veins are few and mild until complications develop. Thus the patient may present complaining only of the cosmetic appearance of the dilated veins or more usually of vague aching and tiredness of the leg towards the end of the day as well as varying degrees of swelling of the foot or ankle, often worse in warm weather. Not infrequently the complaints of pain, cramp or fatigue are disproportionate to the degree of varicosity. In such instances the examiner must be careful to exclude some other organic basis for the complaints such as sciatica, obliterative vascular disease, diabetic or other neuropathy and orthopaedic disorders of the feet or spine. Occasionally varicose veins occur in overworked individuals, especially women, and the complaints in the legs are manifestations of general fatigue rather than of pathological changes in the incidental varicosities. The desire for cosmetic relief may influence some patients to exaggerate the complaints which tend to be numerous in the presence of minimal varicose veins. Generally speaking, primary varicose veins are relatively symptomless and the symptoms of secondary varicose veins are commonly those of the [illegible]

Local exa[illegible] tion [illegible] expos[illegible] the distribution of the involved vein is noted and the presence or absence of nutritional changes and oedema is recorded Should cyanosis, oedema or ulceration be present the possibility that the varicose veins are secondary to an antecedent iliofemoral thrombosis is very likely The course of the saphenous veins should be carefully palpated

such as garters and girdles have been blamed for precipitating or exaggerating varicosities. The effects of trauma, infection and tobacco are too vague to merit serious consideration.

Secondary or compensatory varicose veins are most frequently one of the late complications of iliofemoral thrombophlebitis although any factor causing proximal venous obstruction may overload the saphenous circulation and be followed by varices. Pregnancy might be better discussed here as well as intrapelvic tumours of the uterus, ovary or rectum, all of which



A FIG 368 B

(A) Plain and (B) infra-red photographs of young man with varices due to arterio-venous fistulae of left leg

obstruct free deep venous return and so encourage compensatory dilatation of the superficial veins may be present in association with an arterio-venous fistula and a unique type of varicose vein has been described in which there are multiple, small, direct arterial communications between the femoral artery or its branches and the long saphenous vein in the groin[17] (Fig. 368A and B) Although such connections doubtless exist their frequency and importance in the development of varicose veins have been greatly exaggerated, a point borne out by the reluctance of pathologists to particularise on the nature of the anastomotic vessels. It is not at all improbable that, regardless of whether

from an old or recent deep venous thrombosis will furnish a history of pain, swelling or cyanosis of the limb in pregnancy or in the puerperium or after operation Although in most such an incident is remembered, in many there seems to be no such history, but complaint of bursting pain in the calf on standing, or oedema, or cyanosis with or without skin changes or ulceration suggests deep venous insufficiency. Should doubt still remain the superficial veins are compressed by means of a firmly applied one-way-stretch elastic bandage from the toes to the knee and the patient is taken for a brisk twenty-minute walk. Pain in the bandaged leg develops if the deep circulation is so severely impaired that its function has been performed largely by the compensatory superficial varices, now prevented from filling by the elastic bandage. The test only reveals obstruction of the deep veins, a situation that is found seldom in the stage of chronic deep venous insufficiency since by that time the previously obliterated ilio-femoral trunk has recanalised as a valveless channel. These patients tolerate obliteration of the superficial veins without discomfort. Indeed if they did not one of the most important features of the management of the post-thrombophlebitic state, the firm elastic bandage, would not be possible The compression bandage test and its modifications are of limited value but may be performed when deep venous patency is in doubt.

The competence of the sapheno-femoral valve may be determined by the Brodie-Trendelenb [illegible] the patient lies down and the leg is elevated. If the varices empty immediately *there is no* organic venous obstruction. Digital pressure is then applied over the termination of the long saphenous vein just below the fossa ovalis and the patient is asked to stand, the pressure being maintained. If the long saphenous vein remains empty so long as the pressure is maintained the sapheno-femoral valve is incompetent, the communicating veins are competent and the blood is *flowing through* them in the proper direction, from without inwards. The compression of the long saphenous vein is now released and if the vein fills rapidly from above downwards the sapheno-femoral valve incompetence is confirmed If in spite of the digital compression of the long saphenous vein in the groin the varices fill rapidly when the patient stands, the communicating veins between the deep and the superficial veins are incompetent so that flow *through them* is reversed; it is from within outwards. Even in such circumstances release of the finger compression will occasion an immediate and appreciable increase in venous dilatation in those cases in which the sapheno-femoral valve is incompetent as well. These tests are of limited practical value since more than 90 per cent. of patients presenting with varicose veins have sapheno-*femoral incompetence* and the majority *of the* remainder have incompetence which may for reasons of interpretation be difficult to confirm

Perthe's test[15] is a modification of the Brodie-Trendelenburg test in which a tourniquet is used to obstruct the *superficial* veins high in the thigh The

since the veins may be felt when they cannot be seen. The percussion or ballottement test may help to map out the course of the vessels in such instances as obesity. To do this the saphenous vein is tapped lightly in the calf while the fingers of the other hand palpate in the course of the vein proximally. A definite palpable impulse will be felt with each percussion and thus the course of the vein can be mapped out as well as the course of incompetent tributaries. Although the test is also said to indicate incompetence of the saphenous valves a similar percussion wave may be appreciated in the normal limb so that as a test of valvular competency its value is questionable.

In the majority of cases the long saphenous vein is involved as a long trunk varicose in most or all of its length. Similar extensive varicosity may affect the short saphenous vein. Such gross varices may be accompanied by a greater or lesser involvement of the tributaries of the saphenous veins, or the tributaries may be extensively varicose from one segment of the major vein which itself may appear clinically healthy elsewhere, although it seldom is. Not infrequently there are multiple, dilated channels around the ankle and dorsum of the foot or fine spidery dilatations of the cutaneous veins on the dorsum of the foot, the calf or the thigh. These are frequently unaccompanied by varices of the major trunks and even when they are such spidery and worm-like dilatations tend to persist after radical removal of the major saphenous veins.

Before advising treatment it is usual to perform one or more clinical tests designed to give information which may help to indicate the best treatment for the individual in question. Briefly, such tests are designed to determine:

I. The competency of the sapheno-femoral valve.
II. The competency of the communicating valves.
III. The patency of the deep veins, and
IV. The presence of other associated vascular deficiencies.

To take the last of these first, it is necessary to establish the adequacy of the arterial circulation in the limb before advising treatment of the varicose veins. A history of intermittent claudication, coldness and pallor of the foot with dependent rubor and the presence of nutritional lesions all help in this assessment. The peripheral pulses are always palpated and if any doubt still remains regarding the state of the arterial circulation special tests should be employed. Generally speaking, the presence of slight arterial insufficiency does not contraindicate therapy for varicose veins but it may influence the method of treatment advised.

The patency of the deep veins may be determined because there is still some divergence of opinion here between those who advocate non-interference with the superficial veins and those who feel that even in the presence of deep venous insufficiency some form of treatment may be indicated for the incompetent saphenous system. In most instances the patient who has suffered

ng veins appear as bulges or "blow-outs" and can be marked. Usually a econd bandage must be applied from above downwards as the first one is inrolled or the incompetent saphenous system becomes so distended that dentification of additional "blow-outs" is impossible. The term "Saphena varix" is applied to large bulges in the veins usually found at the termination of the long saphenous vein at the groin or the short saphenous vein at the popliteal fossa (Figs 369 and 370A and B).



A FIG 370 B

(A) Posterior and (B) lateral views of a saphena varix of the short saphenous vein at the popliteal fossa This had been operated upon elsewhere as a semimembranous bursa but no bursa was found and the incision was closed.

Venography has no place in the practical approach to varicose veins of the leg It is discussed in Chapter VI.

COMPLICATIONS OF VARICOSE VEINS

If the vague aches and pain and the mild oedema of the ankle or foot associated with varicose veins are excluded, several troublesome complications remain. Generally speaking, however, complications are not common in the primary type of varicose veins but are exceedingly common in compensatory varices, especially when associated with previous deep venous thrombosis. In all probability these complications are dependent as much upon the deranged deep venous circulation as upon the varicose veins *per se*.

patient now exercises and the state of the superficial varices is noted. If they disappear the inference is that the communicating valves are competent in that blood flow is in the proper direction, from without inwards, and that the saphenous valves are incompetent. If the superficial varices become more prominent it indicates that the communicating valves are incompetent and/or that the deep veins of the leg are obstructed.



Fig. 369
Saphena varix at the fossa ovalis

The comparative or triple tourniquet test[14] may be used to determine the precise location of the incompetent communicating veins between the deep and the superficial veins. Three tourniquets are applied sufficiently tightly to occlude the superficial veins, one as high as possible in the thigh, one in the middle of the thigh and one just above the knee Upon standing up and exercising the leg the incompetent communicating veins may be presumed to lie in that segment in which the superficial veins fill in spite of the tourniquet compression or below the knee if the varices distend below the lowest tourniquet. A similar test has been evolved to localise these " blow-outs " by using the highest tourniquet as in the Perthe's test and then firmly bandaging the limb with a crêpe bandage[18] The patient then stands and the bandage is unrolled from above downwards; the sites of the incompetent communicat-

in detail in Chapter XXIV. Briefly, such an ulcer arises classically in the region of the medial malleolus and is surrounded by an area of pigmentation and dermatitis (Figs. 371 and 372). When the short saphenous system is at fault the ulcer may be found in the region of the lateral malleolus. The ulcers vary in size and number and may encircle the whole of the lower third of the leg. The onset of ulceration is usually precipitated by injury to the limb,



Fig. 372
Classical varicose ulcer

and infection, if not already present, is quickly established. Varices are obvious in the surrounding region although induration of the tissues tends to conceal their extent. In long-standing cases of ulceration malignant degeneration of a squamous cell type may develop but such a change is rare. Sarcomatous degeneration has been reported on one or two occasions. Periostitis may develop when the tibia forms part of the ulcer base.

Superficial thrombophlebitis arising spontaneously or following minor trauma to a superficial varix is the commonest form of superficial thrombophlebitis encountered in clinical practice. Discomfort may be considerable with pain, tenderness, swelling and oedema of the leg. The overlying skin is red and local suppuration has occurred. Although pulmonary embolism from saphenous thrombophlebitis has been reported[12] it is an exceedingly rare event. If the superficial phlebitis does continue to extend into the thigh high saphenous ligation should be done as occasionally clot will be found extending into the femoral vein. Such clot must be sucked out and the operation of sapheno-femoral ligation completed.

Varicose eczema or dermatitis is usually present with varying degrees of pigmentation of the skin and oedema of the ankle and, in most instances, *it is the forerunner of ulceration.* The raised intravenous pressure and the stagnation of blood flow leads to anoxia of the capillaries, the skin and subcutaneous tissues as well as the development of tissue oedema and the extravasation of red blood cells into the tissues. The blood haemolyses and



FIG 371
Early varicose ulcer in usual site

the pigment is released in the form of haemosiderin which is an irritant Thus oedema, pigmentation, anoxia and irritation lead to reduced tissue resistance, itching and scratching, and a weeping form of dermatitis extremely prone to secondary infection becomes established. If the cause is not vigorously treated, lymphangitis may occur and also the stage is set for gravitational ulceration to develop.

It is remarkable how severe varicose veins may be without evidence of complication but it has been said that the inevitable consequence of untreated, long-standing varicose veins is " varicose " ulceration. Although opinion is by no means universal it is becoming more generally agreed that in the majority of cases when ulceration exists with varicosity but without evidence of other complication it is a coincidence and not a consequence of the superficial vein disease. Leg ulceration in the presence of varicose veins is discussed

which is exemplified by the fact that more than twenty different substances have been recommended for this purpose. The efficacy of sclerosing agents depends upon the volume of substance used, its strength, the amount of dilution within the vein and whether stasis or activity is advised after the injection The types of vein most suitable for injection fall into three main categories: first, localised varices associated with competent valves in the saphenous system and in the communicating veins; secondly, the superficial cutaneous varices of the spidery type which seldom need treatment for other than cosmetic reasons; and thirdly, when localised varices recur or remain after an adequate high ligation and stripping procedure. The best long-term results are obtained in the second of these categories while in the first and third prolonged relief, or even cure, may be obtained but eventual recanalisation is almost inevitable. The patient should be warned of this before injections are commenced.

We have found monoethanolamine oleate 5 per cent. satisfactory in a volume of 0 5 to 2 0 ml , the latter amount never being exceeded at one sitting. This soapy substance has been found to be non-toxic, an effective endothelial irritant and free from complications even should extravasation occur. The other popular agents employed are sodium morrhuate 5 per cent. and hypertonic solutions of sugar and salt No equipment is needed other than a 2 0 ml. syringe, a 1½-inch number 20 short bevel needle and sterile dressings. A tourniquet is not used but the patient stands with support, or dangles the leg, and once the vein to be injected has been determined the skin is cleansed and the vein is entered. We use the " empty vein " technique so that excessive dilution of the sclerosant is avoided Thus once the vein has been entered the patient lies down, gentle aspiration verifies that the needle is still in the vein and 1 ml of the chemical is introduced slowly. The patient lies quietly on a couch for ten minutes and then a local pressure dressing is applied to the injection site and normal ambulation is resumed. Since the effect of such injections is localised to three or four inches of the vein in the region of the injection a better effect is *obtained* by repeated small injections than by one large injection Also, by using the " empty vein " technique and limiting movements after the injection the greatest concentration and the longest contact with the intima is ensured The incidence of pulmonary embolism *after injection* is approximately 1 in 15,000 but rises to about 1 in 3,000 if prolonged rest is advised since this is conducive to excessive thrombosis, so that after the initial rest the importance of normal activity of the limb must be emphasized Such pulmonary episodes are due to excessive thrombosis spreading to the deep veins or the result of some of the chemical entering the deep veins through a [illegible]
happening which has [illegible]
grade injection techni[illegible]
more than 2 0 ml of any substances are [illegible] saphenous ligation and when
during the [illegible]

TREATMENT OF VARICOSE VEINS

In the present stage of knowledge of the aetiological factors in varicose veins no preventive measures can be prescribed since the patient has no control over his heredity and his posture has been a long habit. It may be possible to delay their development in potential sufferers by advice regarding aggravating occupations although this cannot often be followed. Once varicose veins are established their progress and the development of complications may be prevented by conservative methods of treatment. On the whole varices, once established, tend to progress and some form of treatment must be instituted if progressive degeneration and complications are to be avoided. The measures adopted depend upon the circumstances of the individual case but fall into one of three categories:

1. **Conservative measures.**
2. ***Sclerosant therapy.***
3. **Surgical intervention.**

Conservative measures consist chiefly of adequate elastic support to the limbs at all times that the patient is ambulatory. Satisfactory elastic support is obtained by one-way-stretch bandages or by well-fitted one-way-stretch elastic stockings. Along with this support, periods of rest with elevation of the limbs and the avoidance of prolonged periods of standing without moving are helpful. Conservative measures never effect a cure but may be advised in cases of old age, generalised debilitating diseases such as cardiac failure, diabetes, carcinoma or advanced renal disease, for the residual effects of deep venous thrombophlebitis and in pregnancy. Although pregnancy is not considered by some to be a contraindication to more active treatment it is best to treat women conservatively during pregnancy since the varicose veins may regress remarkably or even disappear after parturition. In arterial insufficiency varices may be the cause of additional embarrassment to the circulation of the limb by adding to the peripheral resistance, particularly in the capillary bed High saphenous ligation can be most beneficial in such cases but stripping procedures, sclerosants and incisions below the knee should be avoided Each case must be considered on its own merits. The same considerations hold in the post-thrombophlebitic limb where the varicose superficial veins are seldom more than an additional burden for an already inefficient venous circulation. In the majority of such cases of secondary saphenous varicosity operative treatment is advised but again sclerosants are never used.

The local injection treatment of varicose veins by chemical sclerosis is indicated in a small group of patients. We do not use it in conjunction with surgery. The successful obliteration of superficial varices by injection treatment depends upon the use of a substance which will destroy or severely damage the intima of the vessel upon which thrombosis will develop with obliteration of the lumen Unfortunately the propensity of the once-obliterated vessels to recanalise limits the usefulness of the sclerosant therapy, a limitation

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the procedure is a signal to stop the injection since occasionally sloughing and an ulcer may follow extravasation of the chemical into the tissues. After the injection some discoloration of the skin overlying the vein is almost inevitable and is due to resolution of the clot in the thrombosed vein which can be felt as a hard cord beneath the skin. When repeated injections are necessary an interval of two weeks is left between them. The recurrence rate after sclerosant methods is high unless their use is limited to those cases in which the veins are small and major valvular incompetence does not exist.



Fig. 373
Example of severe varicose veins which respond poorly to any form of treatment

When the sapheno-femoral valve is incompetent, with or without incompetent communicating veins, operative treatment is the only method which will ensure prolonged relief from or cure of varicose veins. Although there is no uniformity of opinion as to the most satisfactory surgical technique it is accepted by all, as a first premise, that identification and resection of all the tributaries entering the long saphenous vein at the fossa ovalis and "flush" ligation of the saphenous vein at its entrance into the femoral vein are necessary to the success of any operative procedure The technical details of the operative procedures are described below. Suffice it to say here that the most frequently performed procedures are high saphenous ligation with the multiple resection of previously identified and marked "blow-outs" done as an out-patient procedure under local anaesthesia and high saphenous ligation combined with radical extirpation of the long saphenous vein and its tributaries by intralumenal stripping from the ankle to the groin, which is done on the hospitalised patient under general anaesthesia Injection therapy is not combined with either technique except as a "tidying-up" procedure for the occasional varices which may remain or recur at a later date. Such injections are performed when the patient reports back to the follow-up clinic as an out-patient after several months The addition of retrograde sclerosis does not improve the long-term results of the surgical treatment of varicose veins' so that, since hazards attend its use, it is wise not to use it. With these operative methods cure is obtained in the majority of patients while most of the failures will be cured by further local surgical intervention or by

sclerosants. There always remains, however, a refractory 1 to 2 per cent. of patients who defy even the most concerted attacks and for these there seems to be no real answer in the light of our present knowledge (Fig. 373).

OPERATIVE TECHNIQUES

Although there is no unanimity of opinion as to the most effective operative procedure for the radical treatment of varicose veins there is complete agreement that any procedure, to be successful, must include an adequate high saphenous ligation. The object of this is to exclude the varicose saphenous system from the femoral vein in the groin. High saphenous ligation is conveniently combined with radical stripping of the entire long saphenous vein from the ankle to the groin wherever possible or, where this is not feasible, with multiple ligation and resection of the veins—long or short saphenous or both—wherever they communicate with the deep veins as demonstrated by the multiple tourniquet test.

High saphenous ligation is an operation of major character and it should not be performed except in a well-equipped operating theatre. The skin in the groin, previously shaved, is thoroughly washed with Cetavlon and carefully painted with a non-irritant skin antiseptic before drapes are applied. The operation must not be performed in the presence of local skin infection, open infected ulcer or, with rare exceptions, in the presence of superficial phlebitis Under local or general anaesthesia a 5 cm. vertical or semi-oblique incision is made running through the crease of the groin centred 1·5 cm. below and 2·5 cm lateral to the pubic tubercle and just medial to the femoral artery which has been identified by palpation. A vertical incision is preferred to an oblique one especially in fat patients since it permits a far better exposure and so avoids extensive undermining of flaps so often necessary with the oblique incision Such extensive dissections are to be avoided particularly when the procedure is done under local anaesthesia for the danger of haematoma and infection are then greater The vertical incision is in the line of the vessel to be exposed, an important first principle in vascular surgery, and it also avoids division of lymphatic vessels in the region of the fossa ovalis so that the troublesome lymphorrhoea which is occasionally seen after the oblique incision is never encountered

The incision is deepened through the deep layers of superficial fascia to expose the saphenous vein entering the fossa ovalis and the termination of its various branches. These tributaries are [illegible]
most [illegible]
e [illegible]
fi [illegible]
o [illegible]
e [illegible] to rely upon an adequate [illegible] and a complete dissection of the region rather than upon any standard anatomical description. In this [illegible]
As each [illegible]

Occasionally these tributaries may be difficult to identify and then it is best to expose the main saphenous vein in the lower end of the incision, clamp and divide it and then using the divided end as a retractor to dissect from below up. After all the tributaries have been isolated and divided and the sapheno-femoral junction clearly demonstrated the saphenous vein is ligated flush with its junction with the femoral vein. Medium, braided silk is used for this ligature and as a security against its slipping a transfixion ligature is placed 0·5 cm. distal to it. If no stripping is to be done the distal end of the saphenous vein is ligated and allowed to fall back into the wound which is closed with several subcutaneous catgut stitches to obliterate the dead space and the skin is closed with interrupted vertical mattress stitches of fine silk. One million units of depot penicillin are given to every out-patient at the completion of the operation; there is no objection to the operation being done in out-patient circumstances.

When stripping is not done at the time of high saphenous ligation, or in those rare instances when the veins are so tortuous that the stripper cannot be passed, secondary incisions are made in the line of the vein at the points at which incompetent communicating veins have been marked. Usually from two to three additional incisions are necessary. The most frequent sites for these additional incisions are first in the lower third of the thigh where a constant communicating branch exists between the long saphenous and femoral veins, secondly just above the knee where a communication exists between the long and short saphenous veins, and finally a third just below the knee where a constant communication exists between the long saphenous and deep veins of the calf. Although these are the most usual sites for additional intervention there may be "blow-outs" at any level and the whole limb is examined for them Once exposed the segment receiving the incompetent communicating veins is resected and especial care is taken to identify and to ligate the incompetent perforating branch If the perforating communication is not identified and resected, recurrence at that level is inevitable. At the end of the multiple resection procedure the incisions are dressed, crêpe bandages are applied from the toes to the groin and the patient is encouraged to walk immediately, if the operations have been performed under local anaesthesia, or as soon as possible if general anaesthesia has been employed Retrograde injection of sclerosants are not employed in conjunction with these procedures. Such injections are valueless in the presence of incompetent communicating veins, unnecessary when these " blow-outs " are resected in the above manner and not free from complications of severe superficial phlebitis and even deep venous thrombo-phlebitis as a result of leak into the deep veins.[4]

When stripping of the saphenous system is done, general anaesthesia is essential if discomfort and pain are to be avoided and the patient is hospitalised for from three to five days. High saphenous ligation is performed in the manner just described but the distal end of the long saphenous vein is retained and opened and a malleable intralumenal stripper[2, 13] is passed down the vein

to the ankle where a second incision is made just in front of the medial malleolus. Occasionally it is easier to pass the stripper up from the ankle. The vein is then doubly ligated with silk to the stripper just proximal to the acorn and the stripper is pulled upward, or downward, with a slow, steady action (Fig 374). The vein usually piles up on the stripper or it may turn inside out. It may be necessary on occasion to make one or two additional incisions at the sites of large "blow-outs" so that the vein is removed in sections rather than *in toto* This will also prevent haematoma formation at

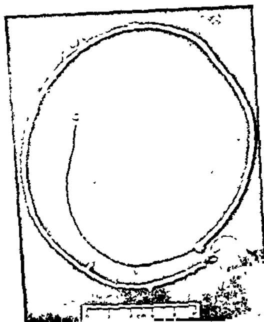


FIG. 374
Malleable stripper with long saphenous vein removed *in toto*

the site of large perforating veins A similar situation may arise when the veins are excessively tortuous and the stripper cannot be advanced below the knee With experience it is usually unnecessary to make more than the ankle and groin incisions since in most patients the main vein is reasonably straight, but with tortuous tributaries

Radical intralumenal stripping leaves a long, bleeding tunnel in the subcutaneous tissues but it is surprising how little bleeding there is and how soon it ceases. All possible clots should be evacuated from the subcutaneous tunnel by milking the limb in its length before the incisions are closed Then the leg is elevated and firmly bandaged from the toes to the groin with six-inch crêpe bandages The limb may be kept elevated during closure of the incisions and bandaging and in this way haematoma formation completely avoided The patient returns to bed for twelve hours and antibiotics may be

administered *prophylactically*. After twelve hours the patient gets up and is usually discharged on the third or fourth day after operation, to be followed-up as an out-patient. It is advisable that the patient wear a one-way-stretch elastic bandage for a few weeks to minimise the transient swelling of the ankle and leg which usually follows ankle to groin stripping.

High flush saphenous ligation and radical stripping of the long saphenous system is considered to be the operation of choice. It gives the highest proportion of good results and post-operative injections for residual veins are not often necessary. It has, however, definite limitations and must not be used in the presence of infection, ischaemic arterial disease, excessive tortuosity or old age. It gives the best results in the early primary varicose veins in younger patients. The short saphenous vein is incompetent alone or in conjunction with the long saphenous system in about 10 per cent. of cases. It is seldom necessary to strip it. It is exposed, doubly ligated and divided through a vertical incision behind the knee joint beginning just below the skin crease over the popliteal fossa.

COMPLICATIONS OF SAPHENOUS SURGERY[11]

The greatest source of complications in the operations designed for the radical cure of varicose veins is the performance of the operation by insufficiently trained surgeons as an out-patient procedure in incompetely equipped operating rooms. There is no doubt whatsoever that retrograde injection of sclerosants definitely increases the complication rate of the operation. Appreciation that high ligation of varicose veins is a major operation to be performed in a well-equipped operating theatre by, or under the supervision of, those especially interested in the subject and that the addition of retrograde sclerosants should be avoided, not only reduces the incidence of complications but also of recurrences. In varicose veins, as in many surgical procedures, the first time is the best time to achieve a cure and the possibility of surgical correction on the second or third try becomes increasingly smaller while the danger and difficulty of the operation becomes increasingly greater

The most frequent complication arising during the operation is haemorrhage, while after operation the most frequent complication is haematoma formation. The latter can be prevented by making sure that haemostasis is complete before the wound is closed, by using obliterating stitches in the subcutaneous tissues and by applying firm dressings and crêpe bandages to the affected limb Should a haematoma develop the incision should be opened and the clot evacuated under aseptic conditions.

Haemorrhage from a torn tributary or from the main saphenous vein itself in the groin can be terrifying, for there may be no competent valves between the sapheno-femoral junction and the right side of the heart. The accident usually occurs while dissection of the saphenous vein and its tribut-

aries is being carried out and the vein is torn or a forceps is pushed through the vein wall. There are few other surgical circumstances in which a cool head is more necessary. Blind, hurried, instrumental clamping must never occur. The best haemostat for the control of the bleeding is pressure by the fingers followed by a pack, and the pressure is maintained whilst a plan of attack is formulated. If the incision is not adequate it must be enlarged and the lighting must be perfect. While the bleeding is controlled by pack and pressure the saphenous vein should be divided distally and the region of haemorrhage approached from below upward. It is seldom difficult to control the haemorrhage temporarily but it may be very difficult to isolate and tie the bleeding point. A ligature slipped up over the saphenous vein will often suffice and if not, judicious clamping may be undertaken only if the bleeding point can be visualised. If it cannot it is often wiser to pack the wound and return to it in twenty-four or forty-eight hours and remove the pack in the operating room under aseptic conditions. This may appear to be an admission of defeat but it is much better than the blind application of clamp after clamp with inclusion of the femoral artery and perhaps subsequent amputation or complete occlusion of the femoral vein and perhaps a permanently swollen leg There is no bleeding at the sapheno-femoral junction that cannot be safely controlled by a pack and pressure.

Ligation of the femoral artery usually follows the blind clamping of vessels in an attempt to stay haemorrhage. In these circumstances, and even during routine exposure, the femoral artery can go into severe spasm and be mistaken for a vein If retrograde injection of a sclerosant is part of the procedure loss of the limb is inevitable. If there is any doubt about the identity of the vessel exposed it should be compressed between the fingers or by a bull-dog clamp while the arteries in the foot are palpated. During the vein dissection the superficial situation and proximity of the femoral artery, and the risk of damage to it, should be constantly kept in mind

Infection of the incisions is not uncommon particularly when the high ligation is done as an out-patient procedure. Excessive undermining of the skin, commonly necessary if an oblique groin incision is used, is the most frequent cause of infection, particularly if haematoma formation occurs. In most instances local hot foments and the exhibition of antibiotics will suppress the infection, but if pus forms the incision must be opened and the wound drained

Some degree of *oedema* of the ankle not infrequently follows the operative correction of varicose veins This is transient and can be controlled by the application of a one-way-stretch elastic bandage for a few weeks, by the end of which time it will have settled.

Deep venous thrombosis, thrombophlebitis and rarely *pulmonary embolism* may follow operations for varicose veins. The incidence of these is greatly increased if bed rest is prolonged after the operation and also if sclerosants are used

administered prophylactically. After twelve hours the patient gets up and is usually discharged on the third or fourth day after operation, to be followed-up as an out-patient. It is advisable that the patient wear a one-way-stretch elastic bandage for a few weeks to minimise the transient swelling of the ankle and leg which usually follows ankle to groin stripping.

High flush saphenous ligation and radical stripping of the long saphenous system is considered to be the operation of choice. It gives the highest proportion of good results and post-operative injections for residual veins are not often necessary. It has, however, definite limitations and must not be used in the presence of infection, ischaemic arterial disease, excessive tortuosity or old age. It gives the best results in the early primary varicose veins in younger patients. The short saphenous vein is incompetent alone or in conjunction with the long saphenous system in about 10 per cent. of cases. It is seldom necessary to strip it. It is exposed, doubly ligated and divided through a vertical incision behind the knee joint beginning just below the skin crease over the popliteal fossa.

COMPLICATIONS OF SAPHENOUS SURGERY[11]

The greatest source of complications in the operations designed for the radical cure of varicose veins is the performance of the operation by insufficiently trained surgeons as an out-patient procedure in incompetely equipped operating rooms. There is no doubt whatsoever that retrograde injection of sclerosants definitely increases the complication rate of the operation. Appreciation that high ligation of varicose veins is a major operation to be performed in a well-equipped operating theatre by, or under the supervision of, those especially interested in the subject and that the addition of retrograde sclerosants should be avoided, not only reduces the incidence of complications but also of recurrences. In varicose veins, as in many surgical procedures, the first time is the best time to achieve a cure and the possibility of surgical correction on the second or third try becomes increasingly smaller while the danger and difficulty of the operation becomes increasingly greater.

The most frequent complication arising during the operation is haemorrhage, while after operation the most frequent complication is haematoma formation The latter can be prevented by making sure that haemostasis is complete before the wound is closed, by using obliterating stitches in the subcutaneous tissues and by applying firm dressings and crêpe bandages to the affected limb Should a haematoma develop the incision should be opened and the clot evacuated under aseptic conditions.

Haemorrhage from a torn tributary or from the main saphenous vein itself in the groin can be terrifying, for there may be no competent valves between the sapheno-femoral junction and the right side of the heart. The accident usually occurs while dissection of the saphenous vein and its tribut-

CHAPTER XXIII

CHRONIC OEDEMA. LYMPHOEDEMA[14]

IT is useful to employ the term lymphoedema to describe those forms of chronic oedema which proceed to a solid non-pitting form, which distinguishes them from the chronic oedemas due to heart or kidney disease; cardiac and renal oedema does not become solid, perhaps because the patient does not live long enough. The term lymphoedema is an arbitrary one and does not necessarily mean that the oedema is due primarily to lymph stasis It is impossible to distinguish clinically oedema due to lymphatic obstruction from oedema due to venous obstruction unless the specific cause is known to be clearly lymphatic blockage on the one hand or venous obstruction on the other Lymphoedema due to lymphatic obstruction becomes solid relatively early, but in very early cases pitting can be obtained (Fig 375) Chronic oedema due to venous obstruction becomes solid relatively late, but a non-pitting stage is reached in due course by all oedema of venous origin So recently as ten years ago a large majority of cases of chronic oedema would be characterised as lymphoedema precox, or spontaneous lymphoedema When a cause is carefully sought, however, a majority of cases can now be ascribed to one or other of the aetiological factors discussed below, but even in cases of chronic oedema which can be traced clearly to a venous thrombosis, or to a series of attacks of cellulitis, or to recurrent incidents of angioneurotic oedema or even to trauma, the oedema seldom remains restricted to the limb first affected, the limb which has been the seat of the aetiological condition originally thought to be responsible for the oedema After a few years, even in these cases, it is usual for the other limb to be affected, and it would seem that in most cases, even when an aetiological factor seems clearly to be



FIG. 375
Pitting oedema.

A not uncommon and sometimes troublesome complication is injury to or division of the saphenous nerve at or near the knee. If it is only bruised or crushed the numbness or loss of sensation in its skin area recovers within a few months, but if it has been divided permanent loss of sensation over the medial side of the ankle and foot results. Fortunately the anaesthetic area tends to diminish with the passage of time.

R. B. L.

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fibrosis in the subcutaneous tissues. There is a sharp upper limit either at the knee or at the groin, though rarely hands and arms and even face have been involved In Milroy's original report, six generations of a family had suffered, twenty-two individuals being affected out of a total of ninety-seven, but of thirty descendants reviewed thirty-five years later, Milroy found only two affected, so that the disease seems to decrease in frequency from generation to generation in affected families

(*b*) **Congenital arterio-venous fistula** gives a hot limb which is longer as well as thicker than its fellow of the opposite side. Limbs so affected in childhood may be the seat of chronic oedema, proceeding to a solid form, in adult life. A patient affected by this form of chronic oedema may give a history of one lower limb having been longer than the other at some period in child hood, but when a patient is seen in adult life, the lower extremities may be of the same length, for although the affected limb grows more rapidly than its fellow, its epiphyses may fuse earlier also in a compensatory way Usually, however, the disparity in length persists in adult life (Fig 376) If the arterio-venous fistulas affect only the soft tissues of the limb there need have been no earlier gigantism in childhood; the length of limb is only affected if there is a fistula on the main artery, or on the nutrient or metaphyseal arteries of the bones of the limb, or within the marrow cavity The affected limb is warmer than its fellow, and there may be spider naevi visible in the skin



FIG. 376
Chronic oedema in a limb (right) also lengthened by congenital arterio - venous fistula.

(*c*) **Congenital lipoedema**[9] is a curious localised adiposity of subcutaneous tissues of lower limbs and buttocks symmetrically. The adiposity is associated with a varying degree of oedema. Like Milroy's disease, this form of oedema may be present already at birth or soon after it, or its onset may be delayed until puberty The degree of associated oedema is not usually gross, and the chief component of the deformity is the adiposity The skin of the swollen part may be tender and scaly Pitting cannot usually be obtained at any stage of this form of oedema The affected parts are often painful and tender to touch.

(*d*) **Diffuse lymphangiomas** in the subcutaneous tissues of a limb may be associated with swelling in the distal part of the affected limb, but the chief

responsible, that aetiological factor has merely precipitated the chronic oedema in a limb which, like its fellow, is in some way predisposed to oedema. In affected limbs there seems to be some local disturbance of the mechanism responsible for the regulation of the passage of water between the vascular stream and the extracellular space.

In chronic lymphoedema of any kind, lymphocytes and later fibroblasts develop in the deeper layers of the oedema, while the superficial layers, greatly increased in depth, remain at first translucent, with large quantities of clear fluid in interstices. In the deeper parts of the subcutaneous space small flakes of lymph lie in turbid fluid and in due course a layer of slow-formed fibrous tissue, laid down first on the surface of the deep fascia, thickens towards the skin. When this fibrosis occupies the greater part of the subcutaneous space, pitting is lost and the oedema is a solid one; when the subcutaneous tissue has been replaced by fibrosis and clotted lymph, the skin thickens also, becomes blue and discoloured in places, and in places proceeds to ulceration.

A suitable classification of causes of chronic oedema might be the following:

1. Congenital.
   (*a*) Milroy's disease; congenital lymphatic fibrous hypertrophy.
   (*b*) Oedema of congenital arterio-venous aneurysm.
   (*c*) Congenital lipoedema.
   (*d*) Diffuse lymphangiomatosis.
   (*e*) Congenital neurofibromatosis with oedema.
2. Allergic lymphoedema.
3. Chronic inflammatory lymphoedema.
4. Post-traumatic lymphoedema.
5. Post-operative lymphoedema.
6. The lymphoedema of erythrocyanosis frigida.
7. Thrombophlebitic lymphoedema.
8. Parasitic lymphoedema.
9. Neoplastic lymphoedema.
10. Lymphoedema artefacta.
11. Spontaneous lymphoedema. Lymphoedema precox.
12. Chylous oedema. Chylous reflux

1. CONGENITAL LYMPHOEDEMA

(*a*) The term "**Milroy's disease**"[6] is reserved for a "**congenital lymphatic fibrous hypertrophy**"[7] which is strictly inherited. It was first observed by Nonne (1891) but was fully documented by Milroy. There is present already at birth, or appears at puberty, a diffuse swelling usually of both lower extremities which pits on pressure at first, but later becomes a solid and permanent non-pitting oedema, with fibroblast proliferation and ultimately

usually the first attack of inflammation occurs in a normal part. The first and later attacks take the form of a superficial inflammation. The skin or mucous surface is red, swollen, hot, painful and tender. There is a low or high fever and an increase in the pulse rate. After each attack of inflammation the local oedema is slower in dispersing than after the previous attack, and finally it may become permanent and indistinguishable from lymphoedema precox. It is always precisely the same surface area which develops the acute inflammatory appearances, though the associated oedema is not restricted to that area and may spread considerably beyond it. When three or four attacks have occurred it is hard to believe that there is not a local tissue predisposition to some organism, and it is hard to believe that a streptococcus is not responsible though the presence of this or any other organism has never been proved. The appearances may be merely due to hypersensitiveness of the subcutaneous tissues of the affected locality to some antigen to which it reacts as it would to the antigens of streptococci. In many cases the oedema is associated with, and the attacks of inflammation wax and wane with, an epidermophytosis of toes or feet. That occlusion of lymphatics plays a part is difficult to prove, though lymphoedema sometimes follows lymphogranuloma inguinale[3] and even tuberculosis of the inguinal glands.

4. POST-TRAUMATIC LYMPHOEDEMA

This form may follow fracture or soft tissue injury of an extremity and has been related also to the post-traumatic osteoporosis of Sudek, but in the latter condition there is a coldness and blueness of the [illegible]ies sometimes [illegible] [illegible]y the swelling [illegible] injury, while [illegible] oedema is due to a sym- [illegible] reflex mechanism, but Telford and Simmons[1] found that it did not respond to sympathectomy. A special and common variety of chronic lymphoedema affects limbs after accidents which have sustained completely circumferential wounds in their upper parts. It is curious that this kind of oedema does not follow the application of free skin grafts in a circular manner over a raw circumferential area in a limb. A pure lymph-oedema, not associated with the Raynaud phenomenon, has been described in workers with compressed air machines. Post-traumatic lymphoedema has a pronounced tendency to slow but gradual spontaneous subsidence, though in some cases a residual lymphoedema of slight degree persists permanently.

5. POST-OPERATIVE LYMPHOEDEMA

Post-operative lymphoedema may follow post-operative thrombophlebitis, and is then indistinguishable from the post-phlebitic syndrome. It may also follow excision of malignant inguinal or axillary lymph nodes. A more

complaint is usually of the localised swelling of the lymphangioma, rather than the distal oedema, which is usually slight in degree. The distal oedema, if it is present, may persist after surgical removal or radiotherapy of the area of the actual lymphangioma.

(*e*) **Congenital neurofibromatosis** may be associated with a certain amount of very solid oedema. The neurofibromatosis itself gives a diffuse thickening of the subcutaneous tissues over a limb but there may be a progressive oedema in the affected area which pits at first and later proceeds to a solid form. There may be café-au-lait spots on the affected extremity.

The treatment of the congenital varieties of lymphoedema does not differ from that of chronic oedema in general. It is perhaps necessary to mention that the removal of individual spider naevi from the skin of patients affected by congenital arterio-venous fistula will do nothing to correct either the girth or the length of an affected limb. In such a limb the abnormal arterio-venous communications are probably very numerous indeed.

2. ALLERGIC INFLUENCES IN LYMPHOEDEMA

An angioneurotic oedema (Quincke's disease), if it comes in frequent attacks, may in due course leave the affected part oedematous between attacks, and sometimes this chronic oedema proceeds to a solid and irreversible form. Alternatively, a patient affected by recurrent fleeting oedema in other parts of the body may suffer from a solid oedema of the lower extremities Chronic oedema precipitated or caused by what appears to be an allergic reaction is often unusual in distribution. When the legs are affected, for example, the toes or even the foot may escape. In some patients the chronic solid oedema affects some part of the body other than the lower extremities, the tongue or lips or eyelids for example, or the upper extremities In one of our cases the chest wall was affected after distant intravenous injection of an iodine compound. At least one of our cases lymphoedema which has later proceeded to a solid form has quite clearly begun after the acute swelling of a limb from a severe insect bite. It was notable that even in this case the contralateral limb began to suffer from oedema also after some years, and it seems likely that the insect bite had merely precipitated chronic oedema in a limb whose arrangements for the maintenance of the volume of the extracellular fluid compartment were in any case faulty In cases where an allergic cause is suspected, the swelling in the limb often remains puffy, pitting, and translucent until a very late stage, and procession to a solid form is often slow.

3. INFLAMMATORY LYMPHOEDEMA

This form of lymphoedema is associated with recurrent attacks of erysipeloid inflammation in the skin of the affected part. The leg, or the arm, or the lip, or the tongue, or the eyelid may suffer. Whether the recurrent inflammation is the cause or the affect of the lymphoedema is disputed, but

be demonstrated in aspirated lymph or in the blood, particularly in specimens taken between 9 p.m. and midnight. The scrotum is commonly affected, showing initially a red shiny skin with vesicles containing milky fluid and filariae, associated often with overt inguinal lymphadenitis. There is usually a double hydrocele and concomitant lymphoedema of the penis. When the lower limb is affected the leg below the knee suffers most, with deep sulci at the ankle. The junction of oedematous with normal skin is often sudden. Other rare sites are the labia majora, breast, arms and trunk. Diagnosis is established by blood films, detection of filaria in aspirated lymph or hydrocele fluid or by complement fixation tests. In treatment, scrotal skin may be widely removed with re-clothing of the penis and testes by skin flaps taken from the dorsum of the penis and the base of the scrotum.

9. NEOPLASTIC LYMPHOEDEMA

This, in its most typical form, is seen in the elephantiasis of the arm which sometimes complicates cancer of the breast. It is due to blockage of axillary lymphatics by malignant tissue, but is often exaggerated and is indeed most commonly seen after radical amputation or high-dosage irradiation of the axilla. It almost inevitably follows the radical amputation for cancer of the breast if the axillary vein is ligated as well as the cephalic. The limb swells to a great and painful size, its joints cannot be flexed and sometimes amputation is the kindest treatment. Lymphangiosarcoma may arise in the "elephantiasis chirurgica" which follows removal of the malignant breast,[13] but has not been reported in other forms of lymphoedema, though I have seen one instance of haemangiosarcoma develop in a limb the seat of a chronic solid oedema. Lymphoedema may precede the multiple tumours of Kaposi's disease (q.v.)

10. LYMPHOEDEMA ARTEFACTA

Chronic solid oedema may develop in a limb the seat of oedema artefacta self-induced by the application of a constricting band. The band may be applied by the hysterical patient either to one or to both sides and the oedema may proceed to a solid form, the swollen limb being of a huge size, comparable with the elephantiasis of the parasitic disease. This variety in the less intelligent hysterical patient has sometimes a sharp upper limit, often marked by a constriction groove, but many modern patients avoid the constricting ring by applying a soft bandage or elastic tissue circularly round the limb at different levels on each occasion so that the transition from the normal to the giant limb below is a gradual one. This is the only form of chronic oedema which affects the soles of ambulant feet, sometimes an important distinguishing feature. This kind of chronic oedema, when it reaches a solid state, and the superficial tissues of the affected part are thrown into giant folds, the skin presenting a pitted and leather-like texture, can make for great difficulty in diagnosis unless the possibility of artefact is kept in mind. I have

directly post-operative variety has been described after an operation for femoral hernia, without post-operative thrombosis.

6. THE LYMPHOEDEMA OF ERYTHROCYANOSIS FRIGIDA

Boyd[22] records erythrocyanosis frigida as the commonest cause of lymphoedema in young women. There is no question that those who suffer from this disease have usually thick legs, especially during attacks of erythrocyanosis. The oedema is always greatest in immediate relationship with the nodules of fat necrosis in the subcutaneous tissues. These patients are, however, liable to develop a chronic oedema which in due course proceeds to a solid form.

7. THROMBOPHLEBITIC LYMPHOEDEMA, POST-PHLEBITIC (LOWER LEG STASIS) SYNDROME[12]

Lymphoedema may persist for six months or a year after a puerperal, post-operative or spontaneous white leg, and many cases of apparently spontaneous lymphoedema have been regarded as post-phlebitic because of an appearance in the descending venogram. The cause of the oedema in these cases is variously ascribed to continuing deep vein obstruction, to incompetence of communicating veins or to recanalisation of a thrombosed deep vein with loss of its valves. Many of the venograms used to illustrate these arguments are not conclusive; in a normal limb the opaque medium sometimes flows back from a point of injection in the femoral vein to below the knee. If these patients are followed for a considerable period, it is not uncommon to find that the contralateral limb which has not been the seat of overt thrombosis, and in whom no vein defect can be demonstrated, in due course suffers the same chronic oedema, sometimes commencing only many years after the onset of oedema in the limb first affected. Even in these patients it would seem that there is a peculiar liability of the limbs to oedema, and that the venous occlusion merely precipitates it.

8. PARASITIC LYMPHOEDEMA

The parasitic form of lymphoedema is due to blockage of the lymphatics of a part by *Filaria (Wuchereria) bancrofti or malayi*. The immature parasite, a microfilaria, is transmitted by the bite of a mosquito, usually Culex, penetrating the skin. This reaches the lymphatic system, where males and females attain sexual maturity in six months and microfilaria hatch out The infected lymphatics undergo inflammation and fibrosis. It is contested whether this is due chiefly to the products of the living or of the dead worms, or to the secondary pyogenic infection which is commonly present. The disease occurs in damp tropical climates. Usually it starts in adolescence with recurrent acute lymphangitis, each attack leaving an increasing oedema, but in older patients the onset may be gradual, without lymphangitis or systemic disturbance. In the acute phase there is pyrexia and lymphangitis and the microfilaria may

The former method shows the rate of lymph drainage from a part, wh latter outlines the actual lymphatics.

Kinmonth found that in all of ten " normals " patent blue was trans from the site of injection to the site of operation. Of ten post-phlebitic the dye was transmitted in eight, and of fourteen lymphoedematous li was transmitted in only two. The actual state of the lymphatic vesse examined by direct inspection after patent blue, or by radiography diodone injection, in sixteen patients suffering from lymphoedema. In (one of them an infant) the lymphatic vessels were enlarged and to failing usually to transmit dye, and in the other eight the lymphatic had a normal appearance. Kinmonth *felt tempted to regard the ab vessels as the lymphatic counterparts of varicose veins.*

Kinmonth also examined, with Kitchin, the capillary filtration the clinically normal forearms of fifteen patients who suffered from oedema of the lower extremities. The rates were normal in seven, but to almost double in the remaining eight, and *these generally the ones lower extremities were most swollen.* It is not yet technically poss *measure accurately* the capillary filtration rate in oedematous limbs, b possible that in some cases the swelling may be at least in part relat fault or *faults in the capillary* filtration mechanism.

12. CHYLOUS OEDEMA. CHYLOUS REFLUX

Rarely lymphoedema of the lower *extremities is associated* w appearance in the skin of the thigh and lower abdomen of *vesicles fill* milky *chyle.* The lymphoedema *here seems* due to reflux of chyl incompetent abdominal lymph vessels. It can be cured by ligation chyle-filled femoral or pelvic lymphatic *trunks.*

THE TREATMENT OF CHRONIC OEDEMA

The treatment *of lymphoedema* is not satisfactory. Certain varieties of treatment *may be of advantage* in specific [illegible]

[illegible] and Arnott[1] have *reported* marked relief of oedema in one case after *the exhibition* of such drugs they have reached a solid form they can be controlled by cortisone or but as soon as these drugs *are stopped* the swelling returns within a f and it is impracticable to continue *treatment indefinitely.*

All lymphoedemas *at* a pitting stage can be *satisfactorily* treated in bed, elevation and massage of the swollen limb *until the oedema* di and subsequent elastic bandaging. An elastic stocking may be wor worn should extend from toes to groin and be supported by a susper Sympathectomy *has no* success in lymphoedema, *except* occasional

known a patient have both feet so affected by this kind of oedema that one was actually amputated, the patient complaining constantly of its unbearable pain and the foot in fact being of no value for ambulation. After the amputation, the contralateral limb, in spite of the presence of a solid oedema at the time of operation, returned quite rapidly to its normal size, the solid oedema disappearing. Artefact was never proved, but there could hardly have been any other explanation for the remarkable cure.

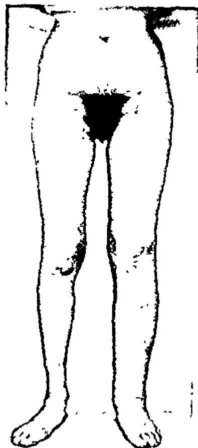


FIG 377
Lymphoedema precox Spontaneous lymphoedema

11. SPONTANEOUS LYMPHOEDEMA

The spontaneous lymphoedema of Telford and Simmons[1] (Fig. 377) is identical with the lymphoedema praecox of Allen, Barker and Hines.[14] The greater the care taken to distinguish separate varieties of lymphoedema, the fewer patients will fall into the spontaneous category. Females are more commonly affected than males in the proportion of 2 : 1. The onset is usually at puberty, but the described age limits are nine and twenty-five years A spontaneous puffiness appears in foot or ankle, unilateral in 70 per cent. gradually extending up the leg over a period of months or years and rarely spreading to the abdomen or flank. Elevation at first produces a temporary disappearance of the swelling, but quite quickly the swelling, though relieved by rest, persists to some extent after it. The skin, at first smooth, may later become roughened and coarse, and the oedema, pitting at first, later fails to pit. Inflammation is rare in such a leg, and the ulceration which may affect a thrombophlebitic leg does not occur. The disease is slow, but " progressive and relentless," and the conditions which make for oedema are probably present in the tissues above the oedematous area, for oedema has appeared in the stump above amputation level a little time after amputation. Kinmonth[3] has made a special study of this form of lymphoedema by the outlining of lymphatic trunks. He has used two methods for this. In the first he injects 11 per cent autoclaved aqueous solution of patent blue[15] into the subcutaneous tissue of the foot or hand and inspects the lymphatic vessels, with their blue fluid content, at a groin dissection during for example the operation of saphenous ligation, or in the dissection of the axilla at a removal of breast. The second method is radiological, the limb being X-rayed after injection of diodone directly into lymphatic channels rendered visible by patent blue.

there is often sufficient skin available to cover by split skin grafts the underlying muscle of the affected extremity, whose girth is greatly reduced by the removal of the superficial fascia with the skin In a few cases the skin may be so extensively devitalised or ulcerated that a portion of the new cover must be obtained from a distant area (*see* p. 817 for a discussion of techniques).

Gillies and Fraser[27] advise the swinging of a broad pedicle flap from the flank to swollen arm or leg to act as a conduit for the oedema fluid.

In extreme and painful elephantiasis of arm or leg after operations for malignant disease, amputation may be necessary.

I. A.

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thrombophlebitic varieties if they are associated with a cold leg;[16] in these it is thought that arterial spasm may be superimposed on the thrombosis.[17]

In the thrombophlebitic variety ligation of the femoral vein has been frequently performed[18] but is not often permanently successful. Superficial ligation of incompetent communicating veins has been done, but it is difficult to be satisfied that all the incompetent ones have been dealt with. In cases where the swollen leg presents a varicose saphenous vein with hard peri-venous fibrous tissue, the vein may be excised together with the fibrous tissue. In all cases epidermophytosis should be brought under control if it is present, and desensitisation attempted by injection of trichophytin.



FIG. 378
Chronic oedema treated by excision of subcutaneous tissue

In solid oedemas surgery is required. The implantation of silk threads[19] or rubber tubes[20] in subcutaneous fascia is unsuccessful, as also is excision of the deep fascia in strips.[21] The most satisfactory operation is the excision of the subcutaneous tissue which is the cistern in which oedema fluid collects. This was first done by Sir Havelock Charles[22] in 1912 for the treatment of filarial elephantiasis. Charles excised skin and underlying subcutaneous tissue and covered the resultant raw surface by free graft from elsewhere, Poth[23] modifying later the Charles technique by using for replacement the skin removed from the swollen limb as a free graft. Sir Archibald McIndoe[24] raised split-skin flaps from the front of the swollen extremity, bringing them laterally and replacing them over the raw area At a subsequent stage a similar operation is performed on the back of the limb, so that the whole limb is denuded of subcutaneous tissue (Fig. 378). Sistrunk,[25] Ghormley and Overton,[26] and Homans have used hinged flaps of whole skin to cover the raw surface left after excision of the subcutaneous tissues, but the blood supply of such flaps is often precarious. Women are often satisfied if the operation is performed from toes to knee—it gives them shapely ankles below the skirt line There is often, however, an ugly bulge or oedema above the field of operation, and of course the toes remain swollen. Posteriorly the denudation is carried out generally only to the heel; the sole of the foot does not suffer from oedema in these cases. If the skin is widely ulcerated or thickly fibrous, or grossly discoloured, it is removed together with the deep fascia and free grafts are applied directly to the muscle. The free grafts may be obtained from the skin removed from the limb, and even if ulceration has been extensive

the most lowly and unimportant of diseases and its management is usually relegated to the newest house officer. However, in recent years there has been a revival of interest and a better appreciation of the pathological principles underlying ulceration in the leg. With this has come a more enlightened approach to the treatment and rehabilitation of the patients, so many of whom have been considered to be incurable derelicts.

GRAVITATIONAL ULCERS

The term gravitational ulcer is meant to include ulcers arising in limbs the seat of varicose veins with or without the presence of deep venous insufficiency or in limbs the seat of deep venous insufficiency with or without the presence of varicose veins. In some clinics the terms "varicose" ulceration and "venous" ulceration are reserved respectively for these conditions but such differentiation has little merit. The opinion is becoming more firmly established that most cases of gravitational ulceration are due to disturbances of the deep venous circulation in the limb, most frequently secondary to an old deep venous thrombophlebitis.[3, 5, 27, 45] Such an opinion was expressed by John Gay[20] almost 100 years ago when he wrote: "*there are no substantial grounds for accrediting ulcers of the legs with varicose veins, to the diseased veins, in the relation of effect; that, in fact, the varicose ulcer in the sense in which it is usually understood, is a fiction—ulceration, when it exists with varicosity but without other complication is a coincidence and not a consequence of the vein disease.*" Although perhaps in most instances gravitational ulcers are of "venous" rather than "varicose" origin there exists a definite group of patients in which no history or evidence of previous deep venous disease can be determined and in these the ulcer must be considered a direct effect of varicosity.

AETIOLOGY.—The commonest underlying factor in a gravitational ulcer is obstruction or insufficiency of the deep venous circulation in the limb. In those patients in whom no previous history of thrombophlebitis can be obtained attempts have been made to demonstrate a congenital deficiency of the valvular system of the deep veins.[9, 30] Usually a previous attack of thrombophlebitis has been followed in from one to twenty years by a stasis ulcer in the region of the ankle, the result of partial or complete recanalisation of the previously obliterated vein.[17] The process of recanalisation is accompanied by fibrosis or complete destruction of the valves in the deep veins, which affects the ilio-femoral trunk, but also extends into the deep calf veins, i.e. the posterior tibial, peroneal and anterior tibial veins. It is probable that valve destruction is most significant in the relatively unsupported proximal veins than in the calf veins which are well supported by muscles and the fascial compartments. The absence of functioning valves leads to venous back pressure in the recanalised segments, inadequate deep venous return of blood from the leg and ultimately dilatation and incompetence of the com-

CHAPTER XXIV

ULCERATIONS OF THE LIMBS OF CIRCULATORY ORIGIN

NON-SPECIFIC, chronic ulcers of the extremities are almost exclusively confined to the lower legs and the vast majority of such ulcers are caused by a pathological condition of the veins. Although such a generalisation is true there are a number of other causes of ulceration of the extremities which must be differentiated from those of purely circulatory or vascular origin. Leaving these for the time being, leg ulcers of vascular origin may be classified as belonging to one of two main types—**gravitational ulcers** and **arterial ulcers**—both of which are more or less dependent upon several general anatomical peculiarities of the circulation of the legs.[11, 18, 13] First, probably nowhere else in the body does so large a mass of tissue exist with so poor an arterial blood supply, and so little need for one, as in the lower half of the leg and the foot—a part of the body consisting almost entirely of skin, tendon and bone. Secondly, no other part of the body is so exposed to the gravitational effects of the erect posture. Thirdly, and perhaps of lesser importance, most people use the muscles of their legs proportionately less than the muscles of other parts of the body especially the arms. Fourthly the legs and the feet are more exposed to injury than other parts of the body. Finally it has been shown that the inner aspect of the leg has a normally less extensive and poorer arterial blood supply than other parts of the limbs.[11] Thus a relatively avascular region of the body bears the circulatory brunt of the erect posture of man while being excessively exposed to injury and infection. It is little wonder that, should such a circulatory situation become additionally burdened by some derangement or disease of the venous or arterial circulation, a chronic ulcer of serious consequence, not only to the comfort and livelihood of the patient but also, in certain circumstances, to the integrity of the limb, may follow a trivial injury or a minor infection

Ulceration of the legs is an important cause of incapacity and in this country it is estimated that about 0·5 per cent of the population suffer from gravitational ulceration alone[3, 7] The words of Benjamin Bell[10] written almost 200 years ago are still worthy of consideration: "*Meeting with more frequent disappointments in the cure of ulcers than of any other complaint has made me first pay more particular attention to their management—a work that will point out to others a material branch of the profession which for a long time has been much neglected; a subject too that still deserves their attention, and in which useful improvements are yet probably to be made.*" The situation today has not advanced a great deal in many places, an ulcerated leg is often treated as

PATHOLOGY AND CLINICAL FEATURES.—Whether the ulcers are of "venous" or "varicose" origin the morbid anatomical features are so similar that they can be discussed collectively without serious reservation. The pathological changes in the tissues which lead to the end stage of ulceration stem, in the main, from two abnormalities of the venous circulation, namely valvular incompetence and venous back pressure.

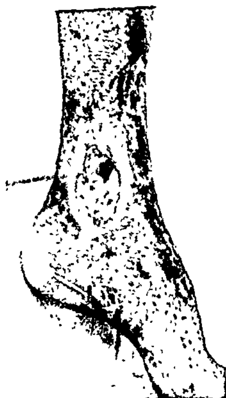


FIG. 380A

"Combined" gravitational ulcer; patient had an ulcer in this situation for twenty years, admitted with gangrene of first and second toes and no arterial pulses palpable below the femoral artery

The increased venous pressure leads to back pressure into the venules and capillaries which become distended, and congestion and stagnation of venous blood flow, as well as anaemia of the vessel walls, which become excessively permeable There is some evidence to suggest that the interstitial tissue pressure increases with the intravascular pressure so that the lymphatic channels are interfered with as well.[29, 30] These changes lead to an increased production of interstitial tissue fluid and to interference with its reabsorption into the circulation so that one of the first results of chronic venous insufficiency is tissue oedema. The oedema is at first mild and disappears overnight or with rest but it eventually becomes persistent, particularly in the presence of deep venous insufficiency The effect of this longstanding oedema is induration, hypertrophy and fibrosis of the skin and subcutaneous tissues which become almost leather-like in consistency. In this final phase the skin is unable to resist the repeated minor trauma of everyday life.

Coincident with the above changes the excessive capillary permeability is accompanied by an extravasation of red blood cells into the perivascular tissues Once outside the vessels, the red cells become haemolysed with the release of haemosiderin into the skin and subcutaneous tissues. This leads to the characteristic coppery-coloured pigmentation of the limb, an almost invariable accompaniment of chronic venous insufficiency. Thus a combination of factors, nutritional poverty, oedema and red cell degredation render a part of the body which is normally under circulatory stress, even more susceptible to trauma and to infection.

municating veins between the deep and superficial venous systems. This may, in certain cases, result in a varicose condition of the saphenous veins, for these are not only exposed to the back pressure from the deep veins, but they are also being called upon to accept an abnormally high proportion of the venous circulation of the limb. Such compensatory varicosity of the saphenous system can occur after any obstruction to the deep venous system.

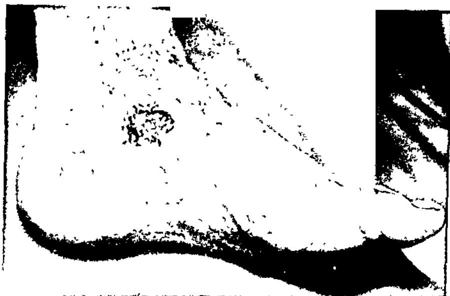


FIG. 379
Gravitational ulcer of left ankle in young woman with congenital arterio-venous fistulae of leg

Varicose ulceration as a complication of primary varicose veins in the absence of other abnormality of the venous system of the leg is not a common condition[3, 27] Such ulceration may arise, however, in a limb the seat of long-standing and extensive primary varicose veins and usually follows some complicating event such as infection or " bursting " and in these the ulcer seems to " ride " upon the offending vein. As in the " venous " type of gravitational ulcer a true " varicose " ulcer is caused by a combination of valvular incompetence and venous back pressure which in this instance is confined to the saphenous system leaving the deep systems of veins competent Sometimes in young individuals with extensive unilateral varices and ulceration of the leg an arterio-venous fistula is present (Fig. 379).

In a small proportion of gravitational ulcers, particularly in the elderly, there may in addition be a chronic arterial insufficiency superimposed upon chronic venous insufficiency.[7] The possibility of obliterative arterial disease should be remembered in any case of chronic ulceration of the leg which does not respond to adequate treatment of the veins Such " combined " ulcers are being encountered more and more frequently in our ageing populations (Figs. 380A and B).

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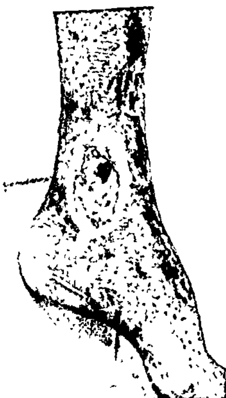


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FIG. 380B
"Combined" gravitational ulcer which originally "girdled" the leg Note exposed tendons, an occurrence never met with in a pure gravitational ulcer.



A FIG. 381 B
Long-standing bilateral gravitational ulcers in the usual site; no history of previous deep venous thrombosis. A—before treatment with ichthyol cream and one-way stretch bandages. B—Five months later

The usual progression of events is that the leg in the region of the ankle becomes itchy and scaly and begins to weep. An eczema or dermatitis develops which may spread rapidly to involve the whole limb below the knee; occasionally the rash appears on the hands and arms as well. In most cases the dermatitis results from the patient consciously or unconsciously scratching and breaking the surface of the skin where the extravasated blood and oedema are most irritating. Ulceration, arising spontaneously or following



Fig. 382
Gravitational ulcer in the classical site

minor trauma to the limb, develops in the midst of the "**stasis dermatitis.**" Occasionally ulceration may occur in the absence of oedema, pigmentation or dermatitis but one or all of these changes are usually present. The classical picture is that of a chronic ulcer just above the medial malleolus lying in the centre of an extensive area of hard, brawny, induration beyond which the skin is deeply pigmented and often scaly and intensely itchy (Fig. 381). Secondary infection of the ulcer is usual and being more common in people of low intelligence and unclean habits the ulcer may become most foul, even infested with maggots

The ulcers of chronic venous insufficiency rarely develop above the lower third of the leg, but occur classically in the region of the medial malleolus because the long saphenous vein and the communicating veins in that part of the limb are most frequently incompetent (Fig. 382). That this part of the limb was especially affected because of its [illegible]

[illegible] alone be involved the ulcer is more likely to be situated on the lateral [illegible] Should the short saphenous

aspect of the lower leg (Fig. 383). Although the ulcer is usually *single, multiple* ulcers may occur and coalesce to " girdle " the lower leg (Fig. 384). The ulcers become fixed to the deep tissues and periosteum, but never transgress the latter to expose the bone or the tendons. The foot is involved only when the patient has gone without shoes so that oedema and venous stasis of the foot have developed; this emphasises the rôle of adequate support in the treatment of the leg condition.

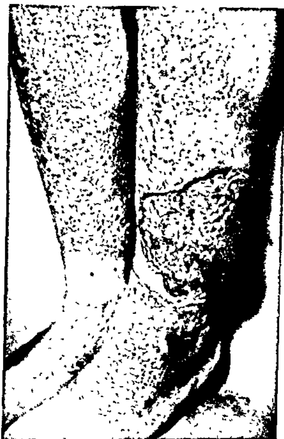


FIG. 383
Gravitational ulcer (post-phlebitic) not associated with varicose veins

The leg in which a gravitational ulcer has become established may or may not be painful. The most frequent complaint is that of a diffuse ache or tightness on the calf of the leg, exaggerated by prolonged standing and often most severe in bed at night The discomfort of prolonged standing is the result of venous congestion and increasing oedema of the leg by gravity and the discomfort at night is due to the increased circulation produced in the limb by sleep. Elevation and rest relieve the discomfort. Severe pain is usually an indication of superimposed infection and cellulitis of an erysipeloid type due to streptococcal infection and lymphangitis, and if these are established severe constitutional reactions are not uncommon Acute inguinal adenitis

occurs and chronic inguinal lymphadenopathy is present in all cases of ulceration True rest pain from association of chronic arterial insufficiency may be added to the discomfort produced by the venous effects. In rare cases the saphenous nerve may be involved in the inflammatory process and neuritis with hyperaesthesia in its distribution may be severe.



Fig. 384
Gravitational ulcer which has "girdled" the leg.

Most patients have conspicuous varicosities in the leg, but in some cases in which varicose veins are present they are contained and concealed by the brawny, indurated skin and oedema and only become demonstrable when the swelling subsides with treatment. The dilated veins are usually seen ascending from the upper edge of the ulcer and in some instances the ulcer may seem to be riding astride a dilated, tortuous feeding vein. Varying degrees of cyanosis of the foot are encountered, most noticeable upon dependency and greatest if the deep veins are insufficient Fungus infections are not uncommon probably because the feet of patients with gravitational ulcers tend to be excessively moist The feet and toes are often abnormally cold; the cause of this is an associated vasospasm with sometimes a fully-expressed Raynaud's phenomenon

The patient is most commonly a woman in the fifth or sixth decade of life although gravitational ulcers may develop at any time from a year onward after a previous deep venous thrombosis The majority of the patients are of less than average intelligence and have little interest in their personal hygiene which accounts for the frequent recurrence and the prolonged duration of ulceration The average duration of ulceration is about nine years and persistence for fifty years is not uncommon There is an unexplained familial tendency in over half of the cases of gravitational ulcer This familial trait

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applies to both the "venous" and the "varicose" ulcer and it is associated with the inheritance of varicose veins; deep venous thrombosis is more likely to occur in a patient with a family history of varicose veins and a patient with a family history of varicose veins is more prone to develop varicose veins and the attendant complications, including ulceration.[3, 4]

The above pathological findings and clinical picture occur in gravitational ulcers regardless of their aetiology and there are no clear-cut features which are exclusive to one or other type. There is little point in attempting to distinguish between the "venous" and the "varicose" ulcer since the factors which produce the ulceration are the same in both and the features of their treatment are similar.

Treatment

"In every species of ulcer, even the most simple, rest of the body, especially of the part affected, is particularly requisite; insomuch that, unless that circumstance be attended to, all the applications that can be had recourse to prove of very little consequence"—Bell.[10]

Briefly stated, the problem in gravitational ulceration consists of getting the ulcer clean, healing it and keeping it healed. The prevention of circulatory stagnation, whether by elevation or by adequate, continued elastic support to the involved extremity, cannot be over emphasised and all other measures must be considered as purely ancillary. The greatest variance of opinion exists upon whether or not the superficial varices should be treated surgically in the presence of previous deep venous thrombophlebitis and, finally, a point too seldom appreciated is that once the ulcer is healed it will inevitably recur unless the co-operation and education of the patient with regard to his disability is stressed.

Most gravitational ulcers are secondarily infected. The discharge should be cultured and if the infection is severe or if cellulitis and lymphangitis are present the appropriate systemic antibiotic should be given. Warm boric acid or saline foments or eusol compresses may be applied locally to help clean the ulcer base. It is seldom necessary or desirable to apply antibiotics to the ulcer itself although favourable reports have followed the local use of tyrothrycin, aerosporin and bacitracin.[7, 9] Once the discharge has been controlled and the ulcer base is clean the medicament which is applied to the ulcer directly is of slight importance so long as it is bland. The one most frequently used in this clinic is ichthyol cream, with zinc oxide ointments next in popularity, but neither can cure an ulcer without the prime measure of adequate rest.

The purpose of rest and elastic bandaging is to remove oedema and to prevent its recurrence, to avoid venous congestion and so to improve the circulation in and the nutrition of the leg. These ends are best achieved by putting the patient to bed with the foot of the bed raised on 12" blocks. Most average-sized ulcers will heal quite rapidly on such a regimen regardless of the local application, the speed of healing being dependent on their size and

chronicity. In large chronic ulcers of long duration it may be necessary to excise the ulcer bed and a margin of the indurated surrounding tissues and apply a split thickness skin graft in order to hasten or even achieve healing. Radical excision of the ulcer and its feeding veins was advocated almost forty years ago[35] and has had a recent return to popularity.[11, 26, 28] We have seldom found it necessary to resort to the operation since conservative measures will always succeed. Although bed rest is by far the most satisfactory method of

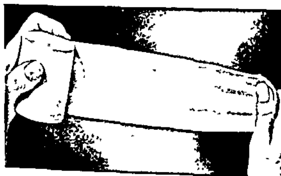


FIG 385

This bandage stretch ... versel ... ins- ... at

resting the limb the patients in whom these ulcers are most prone to develop are seldom economically able to leave their occupations for several weeks or, more likely, there are insufficient hospital beds available for such measures to be universally adopted. In these circumstances the ulcer bed is cleaned by warm, wet foments and a bland soothing cream, such as ichthyol, is applied directly to the ulcer and the surrounding skin at least once a day while the limb is supported throughout the day by a firm, efficient one-way stretch elastic bandage (Fig 385). If the ulcers are showing a tendency to become heaped up a sorbo rubber or felt pad should be cut a few centimetres larger than the ulcer and placed over it beneath the elastic bandage to ensure an even distribution of pressure. This method is simple and is applied by the patient himself, who dresses the ulcer and applies the one-way stretch elastic bandage from the toes to the knee before getting out of bed in the morning. The elastic bandage is left on all day and replaced by a crepe bandage at night (Fig. 386). Crepe bandages alone are of no use since the support they offer is negligible. Elastoplast[13] and Unna's paste boots have obvious disadvantages and are no longer used. There are few gravitational ulcers which will not respond to this ambulatory regimen although in the larger and more chronic ulcers the treatment is prolonged. Fortunately most of these people have lived with their ulcers for many years, sometimes as long as fifty, so that they are at least endowed with, or have acquired, the necessary attribute of patience.

Finally, too, the underlying cause should be treated. Since the primary defect is deep venous incompetence surgical correction of this is rarely feasible, although some attempts have been made,[19, 42] but the incompetent superficial varices should be dealt with by high saphenous ligation with or without stripping.[28] These procedures are best done at the same time as the ulcer is being excised and skin grafted, if such a procedure is necessary, or the veins should be left until the ulcer is clean and healed. There are very few instances

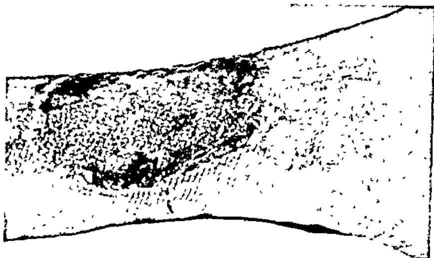


FIG. 386
Healing post-thrombophlebitic ulcer in the usual site

indeed where the presence of previous deep venous thrombophlebitis will contraindicate treatment of the varicose veins which can be nothing but an added embarrassment to an already inefficient deep venous circulation It is surprising how many of these patients have a deep-rooted distrust of surgery and very few of them will accept an operation once the ulcer has healed or shows steady improvement.

We have tried ligation of the superficial femoral[26] and later the popliteal vein,[8, 9] selecting the patients carefully on both clinical and phlebographic grounds A considerable series of both types of procedure has been followed for more than five years and in every case ulceration has recurred. Deep vein ligation will relieve the " bursting " pain in the calf, but so will elastic support properly applied and continually worn. The chief principle of any method of approach to the problem of gravitational ulceration is restoration of an efficient circulation to the limb by adequate support. No surgical measure has been devised which will ensure a permanent cure if elastic support is left off even though the ulcer has healed[12, 26, 36] The avoidance of prolonged periods of standing, rest at frequent intervals with the leg at least horizontal and if possible elevated and the permanent elevation of his bed on 6" blocks are all measures to be practised religiously Such a regimen has been termed " the new way of life."[29] But of paramount importance is the wearing of an adequate

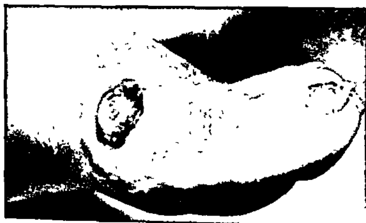


Fig 387A
Chronic arterial ulcer which developed on a bunion; diabetic atherosclerosis



Fig. 387B
Chronic arterial ulcer of toe from pressure of the adjoining toe; atherosclerosis.

one-way stretch bandage or elastic stocking at all times; without this recurrent ulceration will be inevitable. Two-way stretch elastic bandages or stockings are never adequate although they are less bulky and more pleasing to wear. One often finds the one-way-stretch stockings discarded because of their appearance, by women, with the inevitable result. Unfortunately this point is difficult to impress upon patients and once the ulcer is healed they discard all support so that the first trivial injury leads to a recurrence of the ulcer which with each recurrence becomes more difficult to heal.

In an occasional case the association of obliterative arterial disease, Raynaud's phenomenon or excessive sweating of the foot with vasospasm may necessitate the performance of a lumbar sympathectomy. If rigid criteria for such a procedure are adopted some of the patients in whom it is indicated will show remarkable improvement. However, even in these permanent local elastic support to the leg is necessary or ulceration will recur. A more local type of sympathectomy can be performed by crushing the saphenous nerve below the knee[6, 22] This procedure not only increases the local blood supply in the region of the medial malleolus, but also relieves pain in the distribution of the nerve. We have had little experience of such denervation procedures Similarly the local application of physiotherapy and massage to increase the local circulation and break down the fibrosis in the surrounding tissues has not impressed us.[15] It may be simply stated that rest is the only cure and the only practical way of obtaining rest whilst maintaining a reasonably normal life for the patient is by the uninterrupted, constant support of the limb by one-way-stretch elastic bandages or elastic stockings at all times that the patient is not in bed.

ARTERIAL ULCERS

Deficiencies of the arterial circulation to the limbs may result in a breach in continuity of the skin which develops either spontaneously or as the result of trauma or infection. Such ulcers may be considered as "**pure**" when they develop in the absence of any circulatory abnormality other than the obliterative arterial disease which occasions them or they may be termed, "**combined**" when they arise in association with varicose veins or the post-thrombophlebitic syndrome. A "combined" ulcer must always be considered when an ulcer, apparently gravitational, does not respond to the adequate treatment of the venous stasis (Figs. 380A and 380B). Clinically, too, arterial ulcers may be either **acute** or "**necrotic,**" appearing suddenly after an acute vascular occlusion, or they may be **chronic,** developing slowly and persisting in a limb the seat of progressive arterial obliteration.

The underlying obliterative arterial disease is most frequently atherosclerosis which is not uncommonly complicated by diabetes (Fig. 387A). In the younger age groups and when ulceration develops in the upper limbs the usual cause is thromboangiitis obliterans.[32] In contrast to gravitational ulcers the

surface of the tibia

ration is peripheral



FIG. 388

Pre-gangrenous arterial ulcer of great toe in the grossly ischaemic foot of a twenty-eight year old man with thromboangiitis obliterans

present, *i.e.* colour changes, undue coldness, absent arterial pulsation and intermittent claudication. Oedema is not a feature unless secondary infection and rest pain are present, either of which may have driven the patient to *sleep sitting* up or with the leg hanging over the side of the bed. Pigmentation and dermatitis are present only when the ulcer is a "combined" one for then the clinical features of chronic venous insufficiency usually predominate Although the amount of pain varies greatly, arterial ulcers are normally painful particularly when secondary infection is present, as it usually is.

The **acute** or **"necrotic"** arterial ulcer[18] appears suddenly and spontaneously in a limb that may or may not have presented previous evidence of arterial ischaemia. Then actual infarction of the tissues occurs in the territory of an artery affected by the acute spontaneous thrombosis (Fig 389B). Such thrombosis of the smaller arteries of the limbs leads to the sudden appearance of a bluish-red indurated plaque which often shows a fluid-filled bleb over it This plaque becomes black and later sloughs to leave the subcutaneous tissues, tendons and even the periosteum exposed in the base of an ulcer whose edge is well-defined, punched out and often somewhat undermined (Fig 390) An unhealthy grey slough may be present in the floor of the ulcer and granulations are few Although usually single such ulcers may be multiple and since they amount in fact to the first stage of gangrene, progression is the rule and amputation is frequently inevitable

In contrast, the more usual **chronic** or **"indolent"** ulcer[19] of the ischaemic extremity presents a more insidious, but none the less serious, complication of arterial insufficiency The chronic arterial ulcer arises after infection or trivial trauma to the toes or foot. People with chronic venous and arterial insufficiently seem excessively prone to drop objects on their feet, to be stepped



FIG. 389A
Chronic arterial ulcer of the heel which followed a hot-water bottle burn; fifty-eight year old atherosclerotic



FIG 389B
Acute arterial ulcer following acute arterial occlusion, recovered but patient left with foot-drop

upon or to collide with furniture and far too frequently chronic arterial ulcers follow the improper trimming of the toe nails or the paring of corns. Local pressure of the heel on the bed in old people may result in the development of an ulcer on the heel and be the first evidence of a deficient arterial circulation.[40] Once the skin is broken infection is established and if it is not controlled,



Fig. 390
Acute or "necrotic" arterial ulcer of foot in diabetic atherosclerotic, amputated later

especially in the presence of diabetes, *there* is rapid progression to gangrene. These ulcers are small [illegible] infected. Oth[illegible] responsible [illegible] of the ulcer causes its perpetuation and progression.

Chronic arterial ulcers are most frequently encountered in *the seventh* decade of life and, *in contrast* to gravitational ulcers, are predominantly *found* in males. The acute ulcers *similarly* occur in patients in the older age groups and are of short duration, *the* average being a month, *whereas* the chronic arterial ulcers *have* been present for from one to two *years in* most instances before treatment *is* undertaken.[16, 18, 41]

TREATMENT.—The *treatment* of the "pure" arterial ulcer is that of the obliterative arterial disease which is responsible for the reduced blood supply to the affected part. In many instances that means amputation of the limb, but in a considerable number of arterial *ulcers* palliation, or cure, may be

achieved by lesser measures, especially those directed toward the improvement of the collateral circulation.

Most arterial ulcers are secondarily infected so that control of the infection is the first step in treatment. A culture of the ulcer base is obtained and the systemic exhibition of the *antibiotics specific for the infecting organism* is begun. This is combined with the local application of warm saline, eusol or potassium permanganate foments or soaks for ten to twenty minutes three times a day after which the affected part is wrapped in dry, sterile dressings. Local debridement of sloughs may be necessary and often excision of the overhanging edges of an ulcer to prevent " pocketing " beneath them. When this regimen is accompanied by bed rest the ulcer soon shows healthy, pink granulations, at which stage *it may be covered by a split thickness skin graft* or by pinch grafts.[16, 38] If skin grafting is decided against the patient may be allowed to be up and about with elastic support to the limb and a foam rubber pad over the ulcer to improve the circulation and aid healing. The elastic support must not be too tightly applied lest it actually obliterate, as it may do, low pressure collateral blood vessels. The best way to improve the circulation to the limb is to do a lumbar sympathectomy, which should be performed when the ulcer is clean and the infection controlled; in most instances it opens collateral pathways, improves the vascularity of the skin, and leads to early and rapid healing of the ulcer. There are a number of cases in which these measures are not followed by improvement and local or radical amputation must be resorted to. If amputation appears to be unavoidable there should *be no unnecessary delay, for these ulcers are frequently accompanied* by severe rest pain which, if too long continued, may undermine morale and health. Lumbar sympathectomy is the most successful measure in the treatment of arterial ulcers and if performed in time it will cure most ulcers, modify the level of amputation and enable the patient to live with his limb for a few more years before a more radical procedure becomes *necessary*[32]

In the case of a " combined " ulcer in which both ischaemic and gravitational elements co-exist each patient must be dealt with *individually* The *most* difficult aspect of the management of such ulcers is whether or not the incompetent varicose veins should be treated surgically. If there is no doubt that they are embarrassing the circulation in the limb high saphenous ligation is performed and modified stripping of veins only in or above the upper quarter of the leg; no sclerosants are used. Once the incompetent *veins have* been eradicated the ulcer often heals quickly and then the underlying arterial disease should be dealt with if conditions permit. Again lumbar sympathectomy is almost the only measure available, but the increasing scope and application of vascular grafts to replace an arterial segment obliterated by a strictly localised thrombosis is *undergoing critical trial. At the moment* it is too early to say whether the improvement they sometimes give is permanent

ARTERIOLAR ULCERS

Ulceration of the extremities due to disease of the smaller blood vessels supplying the skin and subcutaneous tissues occurs in a variety of clinical conditions Such arteriolar changes may be spastic or occlusive. *It may be that* the latter group is but the end stage of long continued or oft-repeated spasm, a process which may ultimately produce permanent organic obstruction of the vessel On clinical grounds it is best to consider the two groups separately in the first instance at least.



Fig. 391
Hypertensive (Martorell) ulcer of leg of young woman with essential hypertension

Occlusive arteriolar ulceration.—This is encountered most frequently in the absence of arterial or venous circulatory disturbances and in the presence of essential hypertension[1 2 23 31 33] An ischaemic ulcer of the leg occurs in younger hypertensive women whose legs are normal in every respect apart from the presence of a painful, indolent ulcer usually situated on the antero-lateral aspect of the leg about the junction of its middle and lower thirds. There is no evidence of oedema, varicose veins or deep venous insufficiency and all the major arterial pulses are present. The ulcers are not infre[illegible]tly symmetrical and there [illegible]

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haemorrhagic blister. This may [illegible] bluish purple and may be covered by [illegible]
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should be combined with sympathectomy to increase the local circulation and remove at least part of the element of vasospasm, but it must be emphasised to the patient that the operation can only remove one element of the condition and that as yet there is no surgical way of altering the patient's responses to the direct effects of cold and the local susceptibility of the tissues. In a small



FIG 392
Classical chronic chilblains ulcers in nineteen year old girl (*Surgery, Gynecology and Obstetrics.*)

proportion of cases it is impossible to eliminate the underlying influences and the ulcers recur in spite of sympathectomy. In these it may be necessary to advise a change of employment or climate to eliminate the exposure to cold. In chronic, recurrent cases the affected skin and subcutaneous tissues may be radically excised and replaced by split thickness skin grafts from the thighs A few very gratifying results have followed this procedure especially when it has been combined with lumbar sympathectomy.

LYMPHOGENOUS ULCERS

Chronic oedema of a limb is rarely a cause of frank ulceration although a weeping form of dermatitis is frequent (Fig. 393) The hypertrophied extremity may reach an enormous size and be associated with frequent attacks of cellulitis

In fact it might be considered to be the same "in miniature." Biopsy of such an ulcer will reveal the obliterative arteriolar degeneration characteristic of hypertensive arteriolitis. The arteriolar wall is thickened, the lumen is narrowed and hyaline degeneration and intimal proliferation are present These changes may be completed by thrombosis, but this is not common. The resultant ischaemia produces necrosis or infarction of small areas of the skin supplied by the involved arterioles. If no active treatment is undertaken the ulcer will usually heal slowly over a period of several months Healing can always be materially hastened by performing a lumbar sympathectomy which may have to be bilateral. It follows, of course, that the underlying essential hypertension must be treated.

The ulceration of arteriolar spasticity.—This develops as a result of severe, repeated or continued spasm of the smaller arteries of the skin and subcutaneous tissues most frequently of the legs. Spastic ulcers occur in a variety of diseases the best known of which is chronic chilblains discussed in detail in Chapter XVI.[31] Although the ulcers of Raynaud's phenomenon and thrombotic digital artery disease[33] might be included in this category the ulceration which they produce is seldom, if ever, proximal to the fingers and never on the arms or legs These conditions more often lead to fibrosis and sclerosis of the digits, sclerodactyly, rather than to ulceration of the tissues Similar prolonged vasospasm, which may go on to sloughing of the tissue and ulceration if the spasm is not released, may follow cold injuries, nerve injuries, chronic poliomyelitis and the prolonged use of drugs such as ergot. However, most of these conditions are associated with digital gangrene rather than superficial ulceration and when severe nutritional changes are present there is always thrombotic obliteration of the digital arteries.[83]

In chronic chilblains, an effect of local hypersensitivity to cold, multiple, superficial ulcers develop on the lower two-thirds of the posterior aspects of the legs (Fig. 392). The ulcers begin as small, multiple, subcutaneous nodules in the lower, posterior parts of the legs of women often of stout build. The nodules are discoloured, worse in the winter and at first healing in the summer. Eventually the plaques break down to form superficial, indolent ulcers which may exist for years occurring in successive crops, at first healing and then recurring until eventually they remain permanently unhealed. The edges of the ulcers are indurated, the surrounding skin is reddish or cyanotic and pain and tenderness may develop. The limbs are often oedematous and cyanosis, coldness and excessive moisture of the feet are commonly associated The major pulses are all palpable and there is no gross clinical abnormality of the veins of the extremities

There is no specific therapy for such vasospastic arteriolar conditions although sympathectomy will alleviate the symptoms and heal the ulcers First the local areas must be cleaned and kept clean by means of local compresses Debridement of adherent sloughs may be necessary and in some cases split thickness skin grafts may be applied to shorten the convalecence This

Tuberculous ulcers are rare indeed on the limbs and have been confused in the past with the ulcerative stage of chronic chilblains, when they have been called Bazin's Disease Ulcerating cutaneous tuberculides occur most frequently in women who have or have had tuberculosis elsewhere in the body



FIG. 394
Luetic ulceration of leg (A) before (B) five weeks after treatment with local mercury and parenteral bismuth

(Figs 395A and 395B) Painful nodules, sometimes bilaterally symmetrical, develop and break down to form peculiarly indolent ulcers which resist all forms of treatment and, unlike the ulcers of chronic chilblains do not heal with the warm weather of summer The ulcers are often multiple with undermined edges, a greyish slough in the floor which covers unhealthy granulations and from which a thin, watery discharge exudes. The diagnosis can be

and lymphangitis but without actual ulceration of the skin. When definite ulcers occur in an oedematous limb it is usually evidence that there is some other circulatory factor in addition to the oedema, commonly a chronic venous insufficiency which is masked by the oedema. In such cases the chronic oedema follows recurrent bouts of infection in a limb the seat of chronic deep venous insufficiency. With each attack the limb is left more indurated and swollen until it may be difficult to distinguish the cause and effect. The treatment is that of chronic oedema which is discussed in Chapter XXIII for once a limb has become grossly oedematous the more conservative measures, such as those used in the management of gravitational ulcers, seldom cures the oedema or prevent recurrence. Though adequate elastic bandaging controls a few, the majority of patients suffering from gross chronic oedema require some form of radical plastic excision of the diseased tissues, combined with elastic support for an indefinite period after operation.

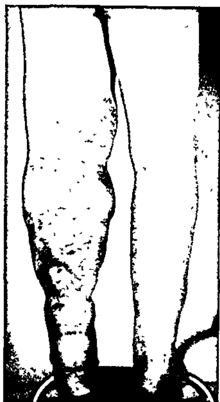


FIG. 393
Lymphogenous ulcer of the leg controlled by one-way stretch elastic support.

MISCELLANEOUS ULCERS

There are a number of causes of ulceration of the limbs which must be differentiated from those of purely vascular origin. Fortunately most of these are uncommon and they can be differentiated fairly easily from the ulcerative lesions of venous, arterial or arteriolar insufficiency.

Syphilitic ulcers are a rarity now because of the effective public health measures and treatment now available Although specific ulcers may appear anywhere on the limb they most commonly affect the upper part of the leg in the region of the knee (Fig. 394). They begin as painless nodules which break down to form multiple, circular or crescentic painless ulcers which are deep, punched-out with an indurated edge, an offensive odour and a necrotic slough in the floor Healing is slow and a thin, tissue paper scar remains to mark the site. Other manifestations of tertiary syphilis are often present and the Wassermann reaction is positive in most, though not in all, cases. In doubtful cases other tests, *i.e.* Kahn, Hinton, should be employed when the clinical picture is suggestive of specific disease In the British Isles syphilitic cutaneous ulcers are rare. The treatment is that of tertiary syphilis and the ulcers heal rapidly when treatment is begun.

established only if the acid fast bacilli have been demonstrated and cultured or if the guinea pig inoculation is positive since biopsy of the ulcer alone may be confused histologically with chronic chilblains in its ulcerative phase " The treatment of ulcerative cutaneous tuberculosis is the treatment of tuberculosis in general, preferably with a sanatorium régime and streptomycin.

Neurotrophic ulcers develop in limbs affected by the neurogenic lesions of tabes dorsalis, syringomyelia, leprosy, nerve or spinal cord injuries, and other peripheral neuropathies, i e. diabetes. These ulcers are usually single and occur



FIG 396
Malignant degeneration in a gravitational ulcer; proven histologically and treated by below-knee amputation

over pressure points such as the sole of the foot beneath the heads of the first or fifth metatarsal bones or over the heel. The ulcer is deep, peculiarly painless and insensitive and involves tendons and bone, which may be seen in its base. The insensitivity of the ulcer, and the patient towards it, usually renders the diagnosis obvious In any peripheral ulcer of the extremity the importance of a neurological examination cannot be over emphasised Such an ulcer on the upper extremity is almost always due to syringomyelia The treatment in each case is that of the underlying disease of the nervous system.

Mycotic ulcers are usually confined to the toes and the feet and should seldom be confused with other causes of ulceration in that region. They are multiple, "ring-worm" in appearance and very itchy, and fungus infection between the toes or in the groin is invariable The treatment is that of fungus disease Patients suffering from chronic oedema and varicose eczema not infrequently have superimposed fungus infection probably because the

suggested but we have not found it.



FIG. 395A
Proven tuberculous ulcer of the ankle. This responded rapidly to systemic streptomycin.

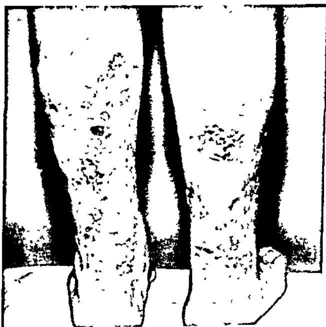


FIG 395B
Ulcerated chronic chilblains

gravitational ulcers in character and site but are not associated with the other manifestations of chronic venous insufficiency. The diagnosis may be established by the blood picture and palpation of an enlarged spleen or the presence of lymphadenopathy. Since these ulcers are usually associated with splenomegaly and hypersplenism the term **splenic ulcer** has been applied to them. Many of these ulcers, most particularly those associated with hemolytic anaemia, heal very rapidly after splenectomy and the remainder improve with the therapeutic measures necessary to the blood dyscrasia at hand. Ulcerating lesions of the extremities may follow the prolonged use of **drugs** such as bromides and arsenicals. These are rare now and if suspected they will heal quickly when the responsible drug is eliminated. **Vitamin deficiences,** chiefly vitamin C, may be associated with ulceration of the legs. In elderly people living alone such a condition must be remembered and the exhibition of large doses of the missing vitamin leads to a rapid cure. **Orf** is a rare cause of ulceration of the limbs and it should be excluded in any patient exposed to sheep or their products, *i.e* shepherds and hide and carcase handlers.[24, 57]

There are undoubtedly many other causes of cutaneous ulceration of the limbs, but only those which are encountered from time to time in the peripheral vascular clinic have been mentioned It should be re-emphasised that the vast majority of patients presenting with chronic ulcers of the legs are suffering from chronic venous insufficiency and this must be excluded before any other diagnosis is entertained.

R. B. L.

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Simple **pyogenic** ulcers may develop in a limb with a normal blood supply but which is unclean. Such ulcers are not uncommon following the infection of excoriations attending pediculosis, a not infrequent finding in overcrowded institutions. Pyogenic ulceration of the legs is not *infrequently* a complication of ulcerative colitis and such a pyoderma heals rapidly after colectomy. These causes of ulceration should not be difficult to diagnose. Similarly a self-



Fig. 397
Sarcomatous ulcer of the leg

inflicted ulcer is occasionally encountered. Such ulcers are always in accessible parts of the limb and should one be suspected a rapid cure follows encasement of the part in a plaster of Paris cast.

When an ulcer persists or progresses under adequate therapy **malignancy** must be suspected either in the form of a primary epithelioma or as malignant *degeneration in a chronic gravitational ulcer* (Fig. 396). In these cases biopsy of the edge of the ulcer is imperative. Histologically most are epitheliomas and their treatment is the treatment of skin carcinoma Sarcomatous degeneration in a gravitational ulcer has been reported (Black) (Fig. 397).

Ulceration of the legs is not uncommon in **blood dyscrasias**[21] the most usual being polycythemia rubra vera, *sickle cell anaemia, hemolytic anaemia,* pernicious anaemia and more rarely the leukemias. These ulcers resemble

CHAPTER XXV

ANEURYSM

An aneurysm is a dilatation of an artery or a blood-filled sac communicating with the lumen of an artery; it may be pathological, traumatic or congenital.

PATHOLOGICAL ANEURYSM

The pathological aneurysm is a dilatation of an arterial trunk. The dilatation may involve the whole circumference to give a spindle-shaped enlargement (*fusiform aneurysm*) or only a small segment of the vessel wall which stretches outwards as a rounded bulbous mass (*saccular aneurysm*) occupied often by laminated layers of clotted blood. A *dissecting aneurysm* arises when a patch of intima ruptures, usually in relation to an area of necrosis and haematoma formation in the media, and blood is forced through the intima and the inner layers of the media to lie within the wall of the vessel and to enlarge there as an aneurysm. A *false aneurysm* is the term applied to the collection of blood which lies outside an artery but which retains a communication with the lumen; the walls of a false aneurysm are formed by adjacent structures welded together in a mass of fibrous tissue; the false aneurysm has not, at least initially, a lining of endothelium.

Sometimes, and especially in saccular aneurysm, blood clot is deposited in successive layers from without inwards, reducing the content of blood and strengthening the wall. Sometimes progressive laminated clot finally occupies the whole sac of a saccular aneurysm, with spontaneous cure The aneurysm thus comes to consist of a succession of different layers. Outside the aneurysm proper is a layer of adventitious fibrous tissue Directly within the sac are layers of white laminated clot and within these laminations lies a softer red blood clot and, finally, the true cavity of the aneurysm contains fluid blood which is in direct communication with the arterial lumen.

The relation even of a fusiform aneurysm to its parent artery is often peculiar Very often the feeding vessel enters not at the proximal end of the aneurysm, but at what would appear to be its lateral side, while the draining vessel leaves it, not from the distal pole, but also from the lateral aspect of the aneurysm, opposite the entrance of the feeding vessel. This peculiar arrangement appears to arise from two causes Very often the effect of syphilis or atherosclerosis of a vessel is initially one of elongation, so that the affected artery assumes the shape of a capital S, and an aneurysmal dilatation of the S-bend seems to lie transversely Once this transverse lie of the sac has been assumed, the aneurysm is subjected to a rotational force, the blood stream

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being directed constantly against one wall. This process of rotation carries the orifices of the end of the feeding and draining vessels still further away from their respective poles.

The effects of arterial constriction on aneurysm formation is unexpected. Halstead first showed that when a band applied to the aorta of an experimental animal is occluded incompletely, aneurysmal dilatation occurs on the distal side of the occluding band. It is not known why this should be. The initial effect of the band is to reduce the height of the pulse wave beyond it and bring the pressure within the distal vessel to a fairly constant mean. Perhaps loss of the pulse wave has something to do with the dilatation which that part of the artery undergoes. Another possible explanation may be that a narrowing of an artery produces a nozzle or jet effect in the flow of blood into the distal vessel, the narrowness of the stream through the constriction increasing the force of the jet. Such a jet effect would have a particular influence in aneurysm formation if the jet were directed constantly against the same part of the wall of the distal vessel, as it may be if the vessel is tortuous at the relevant point. Clinical examples of aneurysms which develop distal to constrictions are seen in the aneurysm of the axillary artery which may be associated with cervical rib, and in the aneurysm which sometimes develops in the aorta distal to a coarctation.

The presence of an aneurysm in the line of a main vessel of the limb lessens the flow in the distal part of that limb, and anastomotic vessels open up. If the aneurysm is large, and relatively close to the heart, the heart may undergo hypertrophy and dilatation.

The complications of aneurysm depend chiefly on pressure effects. The aneurysm may press on the main vessel from which it arises, and also on collaterals, so that the circulation to the parts supplied may ultimately become completely interrupted. Adjacent veins may be compressed with venous dilatation and stasis distal to the aneurysm, and even thrombosis in distal veins Sometimes the first symptom of an abdominal aneurysm is a thrombosis in the vena cava or in the veins of one or both lower limbs. Nerves are stretched and flattened, so that there may be paraesthesiae, pain or paralyses. Portions of clot formed in the aneurysmal sac may be detached and carried distally to lodge as distal emboli Rupture may ultimately occur into serous cavities or hollow viscera, or through skin stretched over the surface of the aneurysm

Pathological aneurysms may be due to atherosclerosis, syphilis, bacterial infection or embolism.

Atherosclerosis is the most common cause of arterial aneurysm now that the incidence of syphilis has fallen. Usually in this type of aneurysm the causative lesion is a weakness in the wall at the site of an atheromatous plaque

The *syphilitic* aneurysm is due to an infiltration of the media (p 481)

The *mycotic aneurysm* is becoming increasingly common in patients who, with the help of modern antibiotics, now recover from such serious infections as bacterial endocarditis, pneumonia, typhoid fever and septicemia.

Embolic aneurysms are due to the weakening of the walls of an artery at the site of lodgment of an infected embolus.

The clinical features of an aneurysm are those to be expected from the dilatation of an artery. There is a swelling which exhibits expansile pulsation and which lies in the line of an artery. The smaller the communication between sac and artery the less obvious is the pulsation, and pulsation is slight also if the greater part of the sac of the aneurysm is filled by clot. Pulsation ceases, and the swelling decreases in size, if the artery is compressed at a proximal point. A thrill may be palpable and a systolic bruit audible over the swelling. The pulse is smaller than on the contralateral side and the pulse pressure in the distal vessel is reduced. The pressure of an aneurysm may erode bone; the vertebrae may be eroded by a thoracic aneurysm but the intervertebral discs escape. Nerves may be compressed with irritation or paralysis, adjacent veins may be compressed or occluded by thrombosis and the overlying skin may be stretched and even necrotic. The initial symptom is sometimes a threat to the vitality of the distal part of the affected limb, as a result of pressure by the aneurysm on its parent trunk and on collaterals, or by the detachment of an embolus from the aneurysmal sac to lodge distally.

The *differential diagnosis* depends usually upon the careful elicitation of expansile pulsation or alteration in the distal circulation of the parts supplied by the affected artery. A tumour or inflammatory swelling in close relation to an artery may transmit pulsation, but transmitted pulsation is not expansile, and compression of the proximal vessel does not usually reduce the size of a neoplastic or inflammatory mass. It should be remembered, however, that if an aneurysm is largely filled by clot, it does not pulsate. Such vascular tumours as osteogenic sarcoma may give expansile pulsation and a bruit, but they are not reduced in size by proximal arterial compression; [illegible]

[illegible] underlying aneurysm, the appearances may suggest an acute abscess. An atheromatous vessel, grossly displaced and tortuous as a result of its elongation, may very closely simulate aneurysm, and atheromatous vessels, particularly in the abdomen, often provide a bruit even though no aneurysmal dilatation is present.

THE TREATMENT OF ANEURYSM

If any treatment is undertaken for aneurysm it should be surgical.

Antyllus, in the third century of our era, opened and emptied the sac of an aneurysm, the circulation through the aneurysm being controlled by proximal compression; he then ligated the affected artery above and below the sac, which was packed and drained. In 1710 Anel ligated the brachial artery immediately above an aneurysmal sac, and three months later his patient appeared to be cured. In 1759 an English surgeon, Hallowell, at the suggestion of a colleague, Lambert, first cured an aneurysm by intrasaccular suture.[1] In 1785 John Hunter[2] performed his proximal ligation of the femoral artery in

being directed constantly against one wall. This process of rotation carries the orifices of the end of the feeding and draining vessels still further away from their respective poles.

The effects of arterial constriction on aneurysm formation is unexpected. Halstead first showed that when a band applied to the aorta of an experimental animal is occluded incompletely, aneurysmal dilatation occurs on the distal side of the occluding band. It is not known why this should be The initial effect of the band is to reduce the height of the pulse wave beyond it and bring the pressure within the distal vessel to a fairly constant mean. Perhaps loss of the pulse wave has something to do with the dilatation which that part of the artery undergoes. Another possible explanation may be that a narrowing of an artery produces a nozzle or jet effect in the flow of blood into the distal vessel, the narrowness of the stream through the constriction increasing the force of the jet. Such a jet effect would have a particular influence in aneurysm formation if the jet were directed constantly against the same part of the wall of the distal vessel, as it may be if the vessel is tortuous at the relevant point. Clinical examples of aneurysms which develop distal to constrictions are seen in the aneurysm of the axillary artery which may be associated with cervical rib, and in the aneurysm which sometimes develops in the aorta distal to a coarctation

The presence of an aneurysm in the line of a main vessel of the limb lessens the flow in the distal part of that limb, and anastomotic vessels open up. If the aneurysm is large, and relatively close to the heart, the heart may undergo hypertrophy and dilatation.

The complications of aneurysm depend chiefly on pressure effects. The aneurysm may press on the main vessel from which it arises, and also on collaterals, so that the circulation to the parts supplied may ultimately become completely interrupted. Adjacent veins may be compressed with venous dilatation and stasis distal to the aneurysm, and even thrombosis in distal veins Sometimes the first symptom of an abdominal aneurysm is a thrombosis in the vena cava or in the veins of one or both lower limbs. Nerves are stretched and flattened, so that there may be paraesthesiae, pain or paralyses. Portions of clot formed in the aneurysmal sac may be detached and carried distally to lodge as distal emboli. Rupture may ultimately occur into serous cavities or hollow viscera, or through skin stretched over the surface of the aneurysm.

Pathological aneurysms may be due to atherosclerosis, syphilis, bacterial infection or embolism

Atherosclerosis is the most common cause of arterial aneurysm now that the incidence of syphilis has fallen. Usually in this type of aneurysm the causative lesion is a weakness in the wall at the site of an atheromatous plaque

The *syphilitic* aneurysm is due to an infiltration of the media (p. 481)

The *mycotic aneurysm* is becoming increasingly common in patients who, with the help of modern antibiotics, now recover from such serious infections as bacterial endocarditis, pneumonia, typhoid fever and septicemia.

Embolic aneurysms are due to the weakening of the walls of an artery at the site of lodgment of an infected embolus.

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the adductor canal for the treatment of popliteal aneurysm, arguing that the artery in the region of the sac was usually diseased and liable to rupture at the point of ligature when the inflammation which so commonly followed surgical operations at that time became established. At the close of the eighteenth century Brasdor[3] advocated ligating the main artery distal to the aneurysm to slow the circulation through it and encourage clotting, and about thirty years later Wardrop[4] used ligation of the branches of the distal vessel with the same intentions.

Rudolph Matas[5] returned to Hallowell's intrasaccular operation, elaborating it and adapting it for a variety of situations. After his time the standard operation for the treatment of aneurysm was Matas' obliterative endo-aneurysmorrhaphy. In this procedure, the sac was opened and the orifices of the main artery and of any collateral vessels arising from the aneurysm were closed by suture from within. The walls of the sac were then approximated to each other by suture, obliterating its cavity. In the case of saccular aneurysms the obliteration was carried out in such a way as to close the opening in the main vessel, leaving the lumen of the main vessel still patent. In fusiform aneurysm, the continuity of the vessel was of course lost. Lambert Rogers[6] considers that endo-aneurysmorrhaphy has a particular application to mycotic aneurysm.

Attempts have been made to reduce the size of aneurysms, and to prevent them from enlarging further, by wrapping them in some such material as cellophane but these have not been particularly successful Cellophane ribbon has also been used experimentally to occlude the dog aorta gradually by the fibrosis which it induces,[7] and a method has been applied to distal and proximal occlusion of subclavian aneurysm in man,[8] but partial increasing occlusion of such a vessel as the aorta is not wholly desirable. At least 75 per cent of complete occlusion must be obtained if the flow through the aneurysm is to be adequately slowed; any less degree of occlusion accentuates the jet-like action of the blood stream through the aneurysm and may lead to an increase in size.[9] Other chemical substances such, for example, as diethyl phosphate, obtained in the synthesis of polythene, have been used to produce an irritative reaction around vessels and to occlude them The method has not always been successful in man. Another method of gradual occlusion, which suffered from the same disadvantages, is the application of tantalum to establish an initial partial occlusion which is rendered complete later by polythene applied at the same time[10] The advantages and disadvantages of these occlusive methods have been helpfully weighed by de Takats.[11]

Various methods of inducing coagulation within the sac have been elaborated. Moore and Corradi[12] first introduced intrasaccular wiring, using iron wire and passing an electric current along it to induce clotting Colt[13] elaborated this procedure and recorded many satisfactory results in a series of thirty-two patients; his methods have been re-stated by Borrie and Griffin.[14] Blakemore and King[15] have refined the coagulation methods still further in

their "electrothermic coagulation." Ten metres of fine silver wire are wound on two spools and introduced into the aneurysm by cannula, the centre of the wire being inserted first, so that the whole length coils within the sac and a current may be run from one free end to the other. A supply of 100 volts D.C. is used, and a run through of approximately 3 amps. A heat of 80°C. is generated and is maintained over two periods of ten seconds. This has been shown to induce instantaneous coagulation if the mouth of the aneurysm is small and the entry of the blood not direct. If the mouth of the sac is large and the entry of blood direct and forceful, electrothermic coagulation of the aneurysm is supplemented by endo-arterial occlusion of the feeding trunk; this is effected gradually by the introduction into the lumen of a silver wire coated with the coagulant polyvinyl acetate. Alternatively, constrictive occlusion may be combined with electrothermic coagulation.[16]

All these methods have now given place to excision and grafting. Proximal ligation, for example, is now regarded as applicable only to selective cases of intracranial aneurysm. Even in the case of a saccular aneurysm which has a small communication with its parent vessel, it is only seldom that removal of the aneurysm is possible with repair of the lateral opening in the affected arteries. The arterial wall is so diseased that further aneurysm formation or rupture of the artery is likely to occur, and when this operation is done, the closure of the parent vessel should usually be reinforced by some such material as nylon, terrylene or vinyon-N.[17]

In summary, it may be said that the treatment of choice of aneurysm is excision. In the case of an aneurysm arising from a small vessel that vessel, e.g. the radial or ulnar, may be ligated doubly after removal of the aneurysm and the segment of the vessel from which it arises. For larger vessels such as the popliteal, excision and reconstruction by vein graft is possibly the treatment of choice, though preserved infant aorta has been used successfully for a vessel of this size.[18] In the case of the aorta, excision and replacement by a suitable variety of graft will probably now supplant most other methods of treatment where this management can be applied. Where it cannot be applied there will probably continue to be a place for some form of wiring and electrical or thermal coagulation. Intrasaccular interposition of a vein or other transplant is likely to be chosen if excision of the sac seems likely to interfere with collaterals. Cloth grafts may well prove to be more suitable than homologous grafts of artery or vein, and nylon, terrylene and vinyon-N have been used successfully in this way.[19, 20] Proximal ligation is unlikely to be used except for the treatment of aneurysms of the circle of Willis, and the other methods of treatment of aneurysm will not in the future have much application.

Before excision of an aneurysm, it is [illegible] of the efficiency or otherwise of the [illegible] information about this can often be c[illegible] for collateral circulation can also be elicited. [illegible] Matas tests [illegible] applied and the main artery is obstructed digitally just proximal to the

aneurysm. After five minutes the tourniquet is released but the digital pressure is maintained. If a re-active hyperaemia is obtained in the distal part of the limb it may be assumed that collaterals are reasonably good. Additional information can also be obtained once the artery has been exposed at the beginning of operation. The affected artery is precisely obstructed just above and just below the aneurysm. If the foot maintains its colour and warmth, it is usually safe to proceed with excision. If the foot becomes paler and cooler, the sympathetic supply to the limb may be blocked, and the collaterals tested.

ANEURYSMS OF INDIVIDUAL VESSELS

The *thoracic aorta* is the site of nearly two-thirds of all aneurysms. In the past, the chief surgical interest of aortic aneurysm has been the need to distinguish it from a mediastinal tumour or, if it has eroded through the chest wall, from a subcutaneous abscess or a pointing empyema, but aneurysms situated between the left subclavian artery and the diaphragm may now be surgically explored with some hope of resection and cadaveric graft.[20] The operation is one of immense difficulty and danger. It is perhaps in this site that electric and electro-thermal methods such as those devised by Moore and Corradi, Colt, Borrie and Griffin and Blakemore and King find their most convenient usefulness, but their methods are complicated, are applicable only to saccular aneurysm and are not in general use. Excision and grafting, dangerous as it is, would seem to be preferable and is soon likely to supplant other methods.

Aneurysms of the abdominal aorta are quite commonly of the saccular type Syphilitic aneurysms of the abdominal aorta usually lie at the level of the renal arteries which commonly emerge from the aneurysmal sac; athero-sclerotic aneurysm usually lies distal to the renal arteries. Atherosclerotic aneurysm is more likely than the syphilitic to elongate the aorta, which it commonly angulates to one or other site below the renal arteries.[21] Pain is the commonest symptom, but there may be such pressure effects as dysphagia, vomiting, haematemesis or even paraplegia from spinal erosion and cord compression. The pulsatile tumour must be distinguished from an abdominal tumour merely transmitting aortic pulsation. The normal aortic pulsation may in slender, aged women be mistaken for aneurysm, and atheroma and tortuosity of abdominal vessels without aneurysm may in elderly women produce a bruit or even a palpable thrill. The pulsating tumour may, even if not readily palpable, be visualised on the screen. Vertebral erosion may be radiologically obvious; it is more common in syphilitic than in atherosclerotic aneurysm,[22] so that syphilitic aneurysms are more likely to be painful; in atherosclerotic aneurysm pain is likely to be a sign of impending rupture. When rupture occurs, it may be into the peritoneal cavity, the retroperitoneum or the duodenum.[23] Rupture is attended by collapse, sudden abdominal pain, rigidity and ileus. A slowly leaking abdominal aneurysm is a definite clinical entity, these symptoms coming on gradually in a patient who is known to

have an aortic aneurysm.[24] Before symptoms develop at all, most abdominal aneurysms have a long asymptomatic course. Radiologically, more than 80 per cent. of abdominal aneurysms show plaques, curved lines, streaks or laminated calcification, or an oval or spheroidal shadow. The diagnosis can always of course be clinched by aortography, but this procedure, particularly when performed for the diagnosis of aneurysm, is quite hazardous, and sudden deaths do occur. It is probable that the diagnosis can be made without aortography, and this dangerous procedure should be adopted only in the last resort

Estes[25] has made a careful study of 102 abdominal aortic aneurysms. Ninety-seven were atherosclerotic in origin and the average age of the patients was 65 years Less than 50 per cent. of these were still alive after three years, as against an expected three-year survival rate of nearly 90 per cent. in normal persons of the same age group; less than 20 per cent. of patients with aneurysms of the abdominal aorta can expect to live five years, as against 80 per cent. of persons of the same age not so affected About two-thirds of these patients died from rupture of their aneurysms Kampmeier[26] in 1936 had an even gloomier experience for two-thirds of his patients suffering from aortic aneurysm died after admission to hospital

Since Dubost and his colleagues first in 1951 resected an aneurysm of the abdominal aorta, a number of successful resections have been reported, and the frequency of resection increases now. The less common (syphilitic) saccular aneurysm may be excised with repair of the consequent lateral defect in the parent vessel Fusiform aneurysms and large saccular aneurysms are treated by excision and insertion of a cadaveric aortic homograft.[27] In nearly all cases there is room for a clamp below the renal arteries. It is usually wise to perform a bilateral abdominal sympathectomy. Clamping of the aorta is likely to produce damage to the lower part of the spinal cord if the clamp is left in place for more than three-quarters of an hour, but there is no danger to the cord if the operation can be completed in twenty, thirty or perhaps even forty minutes This period may be increased very substantially by performing the operation under hypothermia Lower thoracic and upper abdominal aneurysms are approached by a left thoraco-abdominal route through the bed of the ninth rib, lower abdominal aneurysms are approached by way of a midline suprapubic route Ten mg heparin is injected into the aneurysm A tape is applied above and below the aneurysm, and sufficient of the sac and of the aorta is removed for the insertion of the graft. The anastomoses are completed by through and through sutures with 0000 arterial silk [illegible] Cooley have [illegible] which [illegible] Moore [illegible] aneurysm of the bifurcation of the aorta successfully

Dissecting aneurysm of the aorta offers particular surgical problems It seems to be due to a degeneration of the media, with haemorrhage into it

from the vasa vasorum. Frequently the intima related to this dissecting haematoma gives way and the dissecting aneurysm then establishes a new communication with the lumen of the aorta. When such a collection is established there may be a massive outpouring of blood, a sudden increase in the size of the intramural haematoma and occlusion of the lumen by pressure from it. This circumstance is usually fatal, though occasionally double rupture occurs at the proximal and distal ends of the intramural haematoma, the patient recovering and presenting thereafter what is virtually a double aorta. Dissecting aneurysm is important in surgery since on the one hand it may mimic an acute abdominal catastrophe,[30] and on the other, by interrupting the aortic flow, may be mistaken for aortic embolism. When the intima ruptures at the site of the intramural haematoma there is sudden pain, substernal or midepigastric or in the back. There may be faintness, dyspnoea, nausea and vomiting and restlessness. The blood pressure may drop alarmingly or may remain at a relatively normal level, and may sometimes even increase The heart may be enlarged from previous hypertension, with a variety of murmurs. Physical exertion and trauma are less important in dissecting aneurysm than used to be thought, but traumatic rupture of the aorta does sometimes seem to occur. The femoral pulse may be obliterated, as also may be the carotid or the brachial pulses;[31] if the dissection proceeds along the branches of the lower aorta, haematuria, anuria, melaena and mesenteric thrombosis may follow. Ninety-five per cent. of dissecting aneurysms rupture through the outer coat of the aorta or into the pericardium, left pleura or mediastinum. The acute abdominal emergencies which most closely resemble rupture of a dissecting aneurysm are acute pancreatitis and mesenteric thrombosis Indeed mesenteric thrombosis may be part of the picture of dissecting aneurysm. The similarity to pancreatitis is greatest when a dissecting aneurysm, rupturing into the mediastinum or retroperitoneal tissues, causes discoloration of the back. If the possibility of dissecting aneurysm is kept in mind, an anti-mortem diagnosis can often be made [32]

Innominate aneurysm is usually saccular. The innominate artery may suffer alone or may be involved in aneurysmal dilatation of the aortic arch The swelling usually presents in the suprasternal notch and above the right sterno-clavicular joint. The sternum and clavicle are sometimes eroded or displaced. The aneurysm may compress the innominate vein to give oedema and cyanosis of the head and neck, the trachea to give dyspnoea, and the recurrent nerve to give hoarseness or brassy cough The brachial plexus may be affected, with pain and paresis of the arm, or the cervical sympathetic nerves with production of a Horner's syndrome. The carotid and brachial pulses on the right side are lessened in amplitude. Little can usually be done in the way of treatment for innominate aneurysm, for the dilatation usually extends to the aortic arch, which is also as a rule diseased. Perhaps coagulative methods have some application here. Certainly distal ligation of the carotid and subclavian arteries, though it may prevent distal embolism from clot

within the sac, does not usually much accelerate clotting within the aneurysm.

Common carotid aneurysm is more common on the right side than on the left It occurs either at the origin of the artery or at its bifurcation, and it is the commonest peripheral aneurysm in women Trachea, larynx, oesophagus or recurrent laryngeal nerve may be compressed, and cerebral anaemia may



FIG. 398
Right subclavian aneurysm

occur from diminution of the internal carotid flow Cerebral embolism may follow liberation of the clot. These patients are usually in middle age and, in general, surgical treatment should be avoided for fear of interruption of the cerebral flow The application of arterial grafts to this site has not yet proved practicable

Aneurysm restricted to the internal or external carotid artery is rare, though these vessels may share in the dilatation of a common carotid aneurysm Aneurysm of the internal carotid artery *in the neck may give a pharyngeal* swelling, which may mimic a peritonsillar abscess So rare are aneurysms in this site that surgery is seldom required for their treatment, and indeed, since most aneurysms of these arteries involve the bifurcation of the common carotid, intervention would usually run a heavy risk of serious cerebral anaemia.

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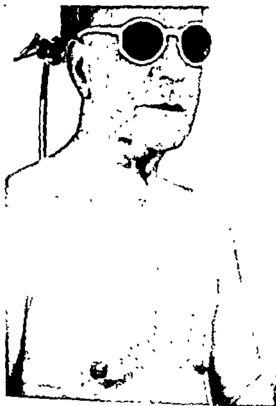


FIG 398
Right subclavian aneurysm

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Subclavian aneurysm used to occur fairly commonly in dock labourers and coal heavers, usually on the right side. Rarely a fusiform dilatation may affect the third part of the subclavian artery distal to a cervical rib. *Pulsatile* dilatation is visible and palpable above the clavicle lateral to the sternomastoid muscle (Fig. 398). This aneurysm is usually fusiform. It may compress the subclavian vein, the brachial plexus or the phrenic nerve, or it may grow down-

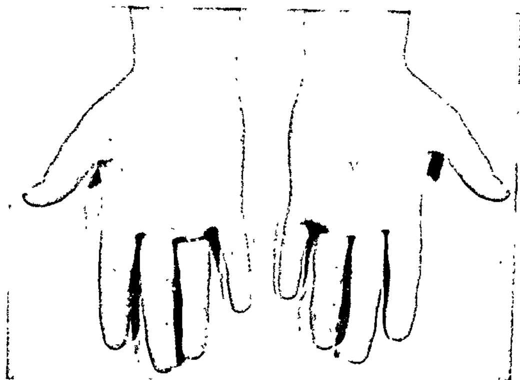


FIG 399
Aneurysm of superficial branch of ulnar artery, with circulatory deficiency in ring finger.

wards into the thorax at the expense of lung Usually it may be successfully treated by proximal ligation, unless the dilatation extends to involve the *innominate artery extensively, or the aortic arch* Ligation of the first part of the subclavian artery is best undertaken by a transthoracic route

Axillary aneurysm is commonest also in men who are labourers, and it too may develop in association with cervical rib Its pressure effects are exerted on the brachial plexus and axillary vein It gives a pulsatile swelling in the delto-pectoral region and in the arm-pit It can usually be satisfactorily treated by proximal ligation of the subclavian artery in the root of the neck

Iliac aneurysm may given a pulsatile swelling of the iliac fossa, but more commonly it enlarges as an *ileo-femoral aneurysm, lying both above and* below the inguinal ligament and sometimes suffering hourglass constriction at the level of the ligament. Oedema, cyanosis, pain, paraesthesiae and paralysis *may occur in the affected extremity* as a result of pressure on the femoral vein and nerve. The ideal treatment of iliac aneurysm is excision

with the insertion of a homograft, but these aneurysms are often adherent and are best treated by a graft inlaid into the lumen of the fusiform sac, which is narrowed around the inserted graft.[33]

Femoral aneurysm gives a pulsatile swelling in the region of the adductor canal. Aneurysm of the profunda femoris is distinguished from it by its failure to alter the distal pulse. Femoral aneurysm may usually be treated successfully by excision, and this is an ideal site for insertion of a vein graft.

Popliteal aneurysm is the most common peripheral aneurysm after the intracranial. It was formerly common in cavalrymen and in post-boys, precipitated in them by frequent extension and flexion of the knee, and often bilateral. Pressure on the tibial and peroneal nerves gives pain and palsy in the leg The popliteal surface of the femur may be eroded, a reactionary effusion in the knee joint is common and the aneurysm may rupture into the joint space Nutritional disturbance and gangrene is more common as a result of this aneurysm than of any other. The "old operation," or extirpation of the sac, is the procedure of choice in popliteal aneurysm,[34] but simple excision with double ligation carries a heavy threat to the nutrition of the foot Linton had a series of fourteen popliteal aneurysms treated by excision with survival of the foot, the excision having been preceded by sympathectomy [35] Blakemore[36] bridged the gap after excision by vein graft inserted with the use of vitallium cuffs, Pratt[37] by vein graft with suture, and by preserved infant aorta [18] Vein graft seems to be entirely suitable at this site, and vein is always available.

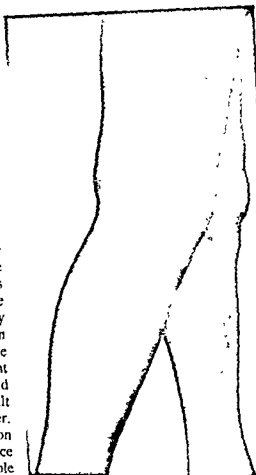


FIG 400
Popliteal aneurysm

TRAUMATIC ANEURYSM

The traumatic aneurysms which follow a single injury, closed or open, are described on page 536.

A special form of traumatic aneurysm is the occupational aneurysm of the palmar arteries [38] This arises not by single severe trauma but by multiple

repeated minor insults to the palmar arch—the repeated shock of a wrongly held rifle, carpenter's plane or electric drill. The resultant lesion is usually a small true aneurysm of the superficial palmar arch; a false aneurysm in this situation is more commonly due to a perforating injury. The true aneurysm may be excised with double ligation of the parent trunk.

CONGENITAL ANEURYSM

Congenital arterial aneurysm may be found in the cerebral vessels, where it may occasion subarachnoid haemorrhage, or in the splenic, renal or coeliac vessels, where it may rupture fatally into peritoneal cavity or stomach. Congenital arterio-venous aneurysm is dealt with on page 745.

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CHAPTER XXVI

ARTERIO-VENOUS FISTULAE

AN arterio-venous fistula or anastomosis exists whenever arterial blood passes into the venous side of the circulation without first having passed through the capillary bed. Arterio-venous shunts fulfilling this definition have been demonstrated anatomically in most organs of the body. In the limbs they are most numerous in the digits, the palms and the soles, where their major rôle is concerned with temperature regulation and heat loss[8] We are not concerned here with these "physiological" arterio-venous communications but rather with those which might be termed abnormal or "pathological" If the above broad definition of an arterio-venous fistula is accepted it becomes apparent that arterio-venous fistulae of the limbs, cirsoid aneurysms, angiomata and glomus tumours are in fact all variants of a common fundamental abnormality[12] Since, by usage, the term arterio-venous fistula has been reserved for congenital and acquired abnormal communications between arteries and veins in the extremities emphasis will be placed on such lesions in this chapter and such conditions as glomus tumours, haemangiomata, etc., which might better be termed "vascular tumours," will be discussed separately

To William Hunter must go the credit for separating the arterio-venous fistula from the arterial aneurysm Observers before him had clearly described the clinical features of the condition but had considered the artery alone to be at fault Hunter described the characteristic thrill and bruit, its abolition by proximal occlusion of the artery and the dilatation of the involved artery entering the fistula It was his opinion that such a lesion was always traumatic, being frequent at that time in the antecubital fossa as a consequence of blood-letting In fact it is only in the last few decades that the high incidence of congenital arterio-venous anastomoses has been [illegible]
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that the passage of arterial blood into the venous system without prior circulation through the capillary bed may result from either a developmental anomaly due to the pathological persistence of congenital communications between arteries and veins or as an acquired lesion following trauma to an adjoining artery and vein anywhere in the body although the limbs are the sites of predilection.

repeated minor insults to the palmar arch—the repeated shock of a wrongly held rifle, carpenter's plane or electric drill. The resultant lesion is usually a small true aneurysm of the superficial palmar arch; a false aneurysm in this situation is more commonly due to a perforating injury. The true aneurysm may be excised with double ligation of the parent trunk.

CONGENITAL ANEURYSM

Congenital arterial aneurysm may be found in the cerebral vessels, where it may occasion subarachnoid haemorrhage, or in the splenic, renal or coeliac vessels, where it may rupture fatally into peritoneal cavity or stomach. Congenital arterio-venous aneurysm is dealt with on page 745

I. A

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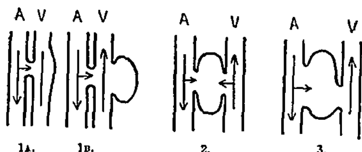
CHAPTER XXVI

ARTERIO-VENOUS FISTULAE

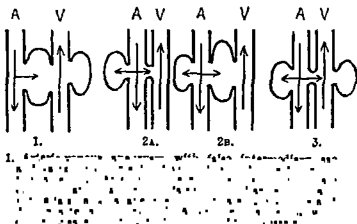
AN arterio-venous fistula or anastomosis exists whenever arterial blood passes into the venous side of the circulation without first having passed through the capillary bed. Arterio-venous shunts fulfilling this definition have been demonstrated anatomically in most organs of the body. In the limbs they are most numerous in the digits, the palms and the soles, where their major rôle is concerned with temperature regulation and heat loss[8] We are not concerned here with these "physiological" arterio-venous communications but rather with those which might be termed abnormal or "pathological" If the above broad definition of an arterio-venous fistula is accepted it becomes apparent that arterio-venous fistulae of the limbs, cirsoid aneurysms, angiomata and glomus tumours are in fact all variants of a common fundamental abnormality[32] Since, by usage, the term arterio-venous fistula has been reserved for congenital and acquired abnormal communications between arteries and veins in the extremities emphasis will be placed on such lesions in this chapter and such conditions as glomus tumours, haemangiomata, etc, which might better be termed "vascular tumours," will be discussed separately.

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has been associated with marked perivascular extravasation of blood which has been circumscribed by the surrounding tissues to form at first a well-defined pulsating haematoma and eventually an encysted sac continuous with the openings in the blood vessels. Very rarely the artery is doubly injured so that in addition to an aneurysmal varix or a varicose aneurysm there may be a true arterial aneurysm of the arterial wall opposite the vein.



1. Arterio-venous fistula without (1A) and the same with (1B), a venous sac—varix aneurysmaticus 2. Arterio-venous aneurysm with false intermediary sac—aneurysma varicosum. 3. Arterio-venous aneurysm with arterial sac. Secondary arterio-venous aneurysm.



1. [illegible]

FIG. 402

(By Courtesy of The Lancet.)

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Depending upon the type of fistula incurred and so the amount of perivascular extravasation of blood, pressure atrophy and a greater or lesser degree of fibrosis develops in the surrounding tissues. The pulsating haematoma, if such is present, becomes excavated into a communicating sac by the development of organisation in its walls which are thickened by the dense fibrous reaction that results from the residual haematoma, and the circumscribing muscles, fascia and bone. The sac becomes lined quite rapidly with endothelium which grows in from the torn edges of the communicating artery and vein. In rare instances, particularly if the fistula is small, thrombosis may develop with spontaneous cure of the condition The vast majority

of fistulae persist and enlarge at first until fibrosis and degenerative changes such as atherosclerosis prevent further progression in *their size*. The sac and the edges of the fistula become atherosclerotic and calcification and even bone formation have been reported. These degenerative changes render any reparative surgery for the defect impractical.

Apart from the actual local effects at the site of the fistula, in the sac, and in the surrounding tissues, well-recognised changes develop in the artery and veins proximal and distal to the fistula. With the passage of time the artery entering the fistula becomes dilated, thinned and tortuous. In some cases the enlargement has become so gross as to fulfil all the requirements of a true aneurysm This aneurysmal dilatation and degeneration of the entering artery has been termed "**venafication.**" Although the most probable explanation of the dilatation is hydraulic because of the greatly increased volume of blood flowing through, if hydraulics alone were operative one might expect a certain amount of work hypertrophy to be present but it is not This suggests that some other factor or factors are operative, the most probable of which is that of nutritional deficiency of the arterial walls, the dilatation constricting vasa vasorum and interfering with the blood supply to the walls of the vessel, so that a vicious circle of increasing dilatation causing an increasing impairment of blood supply is developed.[28, 31] It has also been postulated that the loss of peripheral resistance in the vessel diminishes the amount of recoil and contraction required of it and this may lead to dilatation[1, 25] In contrast to the entering portion of the involved artery the distal segment is usually of smaller calibre than normal although in some instances the retrograde blood flow from collateral vessels back into the fistula may be so great that the artery distal to the fistula becomes dilated as well.[12]

A similar, but more pronounced and rapid, dilatation of the involved vein on the cardiac side of the fistula occurs and eventually the vein becomes thickened as well, a process which has been termed "**arterialisation.**" The hypertrophy is predominantly a fibrous tissue hyperplasia but there is some increase in the elastic tissue in the vein wall. The changes are strikingly similar to those seen in a vein which has been transplanted into an artery as a graft No doubt the changes are again chiefly hydraulic in consequence of the greatly increased volume of blood flow and the high pressure to which the vein is now exposed but the similarity between the changes in fistula and in a vein graft make it difficult to exclude a nutritional deficiency being operative as well. It is a broad general rule that the size of a blood vessel is roughly proportional to the amount of blood flowing through it In short an arterial lumen adapts its size to the requirements of the organ or the situation it is faced with. This thesis is given some support in arterio-venous fistulae where the calibre of the involved artery and vein proximal to the communication is greater in a large fistula than in a small one since the larger the fistula the greater the volume flow through it.

In contrast to the artery distal to the fistula the veins distal to the fistula become grossly enlarged and varicose. The secondary dilatation is predominantly due to the blood pressure in the major vein at the site of the fistula being, for all practical purposes, at arterial level. Two abnormalities result from this. First, the tributary veins become indirectly obstructed and blood is dammed back into them at an abnormally high pressure. Secondly the valves in the tributary veins become incompetent so that succeeding venous segments down the limb dilate, hypertrophy and become varicose. The abnormal venous pressure and the circulatory stagnation accompanying it are reflected in capillary stasis and all the complications of chronic venous insufficiency ensue. Extravasation of red cells into the tissues leads to pigmentation and irritation, and finally stasis dermatitis and ulceration develop. Oedema of the limb and soft tissue hypertrophy and fibrous tissue hyperplasia along with a permanently increased blood volume in the venous bed of the limb result in a chronic enlargement of the whole extremity.

If a fistula in limb vessels is congenital, or if one is acquired before the epiphyses have closed, the chronic enlargement noted above is accompanied by a true increase in length of the bones of the limb. Thus the affected arm or leg becomes longer than its mate. The reason for this has not been settled. If the blood flow through the affected limb is measured it will be found to be greatly increased above that in the opposite limb and the oxygen content of the venous blood will approach that of the arterial blood. The obvious explanation of the increased skeletal growth is that it is a reflection of the increased blood flow to the limb However, lumbar sympathectomy performed in experimental animals is said not to produce any increase in the length of the limb[10] although it has been reported to do so when performed in children whose limb has been left short following anterior poliomyelitis.[11] Since vascular tone is rapidly regained after sympathectomy so that the blood flow to the limb approaches normal preoperative levels it is perhaps not surprising that sympathectomy is a not altogether successful method of producing skeletal hypertrophy and by no means disproves that increased circulation is the cause of bone overgrowth. An attractive possibility is that the muscle hypertrophy may be responsible for the skeletal hypertrophy in the same way that skeletal atrophy in anterior poliomyelitis is directly proportional to the muscle power in the involved limb.[41] The fact that the soft tissue changes in a limb the seat of an arterio-venous fistula resemble closely those developing with chronic venous insufficiency has led to interest into the effect of the relative circulatory stagnation so obviously present. It has been demonstrated that the pH of the blood in a limb with an arterio-venous fistula is more acid than normal and it has been suggested that it is this factor which is responsible for the enlargement of the limb.[38] But artificially produced venous stagnation does not increase skeletal limb growth so that the precise modus operandi of skeletal hypertrophy must remain unsettled at the moment but with the

scales weighted in favour of the increased peripheral blood flow which is such a feature of an established arterio-venous fistula, whether congenital or acquired This is supported by the well-known bone overgrowth consequent upon synovial inflammation, with its increased epiphyseal blood flow, in early tuberculosis of joints. Another cause of bone overgrowth is osteomyelitis when the nutrient artery is thrombosed and the synovial anastomoses hypertrophy to supply the bone and in so doing give an increased epiphyseal blood flow.

CONGENITAL ARTERIO-VENOUS FISTULAE

Developmentally arteries and veins arise from a common vascular anlage and normally there are multiple communications between the arterial and venous trunks, communications which atrophy and disappear in the normal course of development. Occasionally these fistulous connections persist and direct or indirect communications between an otherwise normal artery and vein are carried into extra-uterine life. When the multiplicity of connections between the future arteries and veins are studied in the early embryo it is surprising that their differentiation from the common capillary plexus is not complicated by the more frequent persistence of anastomotic channels. Although congenital fistulae are present at birth they may lie latent for many years before opening up either after trauma or spontaneously. If the abnormal channels are small the effects may be minimal or absent at birth and only become apparent as the child becomes older. In fact the average age for diagnosis of congenital intracranial arterio-venous fistula is forty years so the lesion may be present for many years before causing symptoms. Such a delay is exceptional in the limbs and in this situation cutaneous birthmarks are frequently associated (Fig 403).

The most frequent site for congenital arterio-venous fistulae is the lower extremities where more than half of all congenital lesions occur. The upper extremities, the head and neck, and the intracranial vessels are involved in decreasing order In our experience the leg is involved in 60 per cent. of cases seen and 75 per cent. of our patients are females In the limbs the knee, ankle, elbow and wrist appear to be the sites of predilection. Perhaps this is not surprising since these regions in limbs are associated normally with complicated collateral networks so that there would appear to be a greater risk of persistence of embryological communications in these situations In contrast to the acquired fistulae, a characteristic feature of congenital arterio-venous fistulae is the multiplicity of communicating channels between the involved artery and vein An additional factor which makes their treatment difficult, if not often quite impractical, is the length of the involved segments of vessels

There are two main anatomical types of congenital arterio-venous fistula[37] In the first there are lateral communications between the artery and vein by small anastomotic channels and the continuity of the major vessels is not interrupted In the second the continuity of one or, more frequently,

both vessels is *interrupted*, one or more arteries terminating in a plexus of veins or large venous sinuses. The number and size of the fistulae determine the future course of the lesion. Thus even if the communications are multiple, but small, their growth will be slow which may explain the delayed clinical detection of some of the fistulae. But why an arterio-venous fistula may *remain latent for thirty years* or more cannot be adequately explained [20]



FIG. 403

(*a*) Black and white and (*b*) infra red photographs of the right leg of a 16-year-old boy with an extensive birth mark and congenital arterio-venous fistulae. The dilated venous channels beneath the pigmentation of the birth mark are nicely shown

Generally speaking congenital arterio-venous fistulae may be arterial, venous or arterio-venous depending upon the predominant vascular constituent although at times it is *difficult, if not impossible, to decide definitely the precise nature of the component vessels.*[97] *In this respect it* will be appreciated from the definition of an arterio-venous communication that capillary and cavernous haemangiomata are in fact merely variants of congenital arterio-venous fistulae and not tumours at all. This was known to Virchow who

showed that cavernous haemangiomata of the liver could be injected from the portal or hepatic veins or arteries. Similarly "cirsoid" aneurysms are merely a variant of arterio-venous fistula and although some of them may be congenital the majority of them are felt to follow contusive injury which may have been suffered during childbirth.[7, 23, 31]

All the arterial and venous alterations discussed under acquired arterio-venous fistulae develop to a greater or lesser extent in the congenital lesions. Thus the entering artery becomes enlarged, thinned and tortuous and a *similar dilatation* of the involved vein or veins draining the fistulous site develops as in the acquired form The degree of dilatation depends upon the size and number of fistulous communications which in turn govern the volume flow through the anastomoses. Again there is obstruction to venous drainage and all the clinical features of chronic venous insufficiency are apparent in the limb. In short the cardinal changes in the limb with an acquired or congenital arterio-venous fistula differ in no respect except their mode and rate of onset. Thus the limb the seat of a congenital fistula will show varicose veins, stasis pigmentation and ulceration, and hypertrophy of length and girth all developing for the reasons outlined in the acquired form of fistula. Occasionally the congenital communications may involve the bones of the limb in that the vessels are within the substance of the bones which become eroded.[30] We have seen one patient with a congenital arterio-venous fistula of the leg, which was only diagnosed after a pathological fracture had occurred.

ALTERED CIRCULATORY DYNAMICS

The careful study of experimentally produced arterio-venous fistulae in animals[12, 16, 21] and the detailed clinical and laboratory examination of acquired arterio-venous fistulae,[22, 26, 32-36, 39, 43, 44] particularly in veterans of the recent war, have added to and confirmed the knowledge that such abnormal communications have a profound effect upon circulatory haemodynamics. There are two stages or phases of readjustment in the body The acute phase is strikingly similar to that of acute haemorrhage except that the loss of blood in an acute fistula is chiefly into the capacious venous beds. After the initial shock the body enters into a chronic phase in which there are circulatory readjustments to compensate for the presence of the fistula. This chronic phase resembles very closely the clinical picture seen in free aortic regurgitation

Acute Phase of Arterio-venous Fistula.—The immediate effects of an arterio-venous fistula are best studied in the experimental animal but doubtless occur when an acute acquired aneurysmal varix becomes established *in man* On fortunately rare occasions the clinical picture to be described occurs when a Potts anastomoses for the relief of cyanotic heart disease is performed with the establishment of too large a fistula between the aorta and pulmonary artery

Depending upon the size of the fistula there is an immediate and profound reduction in the peripheral resistance accompanied by an acute reduction in the volume of blood circulating in the arterial tree. The arterial blood seeks the path of least resistance, which is through the fistula into the venous system. In short the patient or animal bleeds into his venous beds and a clinical picture almost indistinguishable from acute haemorrhagic shock is produced. The systolic and diastolic blood pressures fall and the pulse rate is increased.[12] In compensation for the suddenly diminished blood volume in the arterial bed and the transient reduction of blood return to the heart, the heart temporarily decreases in size as do the major arteries of the body.[12, 21] As soon as the body recovers from the initial stage of shock, usually within a few hours, the vasoconstriction gives way to dilatation which is most pronounced in the heart by virtue of the enormously increased venous return via the fistula. The effect of the increased venous return to the heart and the tachycardia, which persists, is to convert the transient fall in output of the heart with the opening of the fistula into a permanently increased cardiac output. To compensate for the loss of circulating blood volume into the venous system there is a recruitment of extracellular fluid which becomes apparent by a demonstrable haemodilution. Thus ultimately there is an increased blood volume, an increased circulation rate and cardiac output with an enlarged heart.

Most of the early changes are similar to those seen in acute haemorrhagic shock and they vary in severity directly with the size and the site of the abnormal communication. For example a large fistula close to the heart may lead to a profound fall in the blood pressure, a pronounced tachycardia, early and progressive cardiac dilatation and rapid death from heart failure. In the more usual peripheral fistulae the organism recovers from the acute phase and certain compensatory alterations in the circulatory haemodynamics become established. Before discussing them some purely local phenomena which are attendant upon the opening of an arterio-venous fistula must be mentioned.

When the fistulous communication is opened experimentally or develops acutely after trauma the pathognomonic thrill and bruit become apparent Both are machinery-like in character, rough, vibratory, transmitted both up and down the limb and although continuous throughout the cardiac cycle a definite systolic accentuation is present. The thrill and bruit are hydraulic in origin being produced by the eddies and currents of blood passing through the fistula under alternatively high and low pressure. Generally speaking the loudness of the thrill and bruit is proportional to the size of the individual fistula and so to the volume of blood flow through it. If the pressure across the fistula is equalised as by proximal arterial occlusion the thrill and bruit are abolished—a point established by William Hunter in 1757.

The limb distal to an acute fistula becomes cold, cyanotic, and oedematous and if sufficient arterial blood is shunted from it, gangrene may develop

Venous engorgement is pronounced because of the greatly elevated intravenous pressure which obstructs proximal blood flow from all veins tributary to the one involved. At first the distended veins are masked by the oedema but become clinically apparent when it subsides in the first few weeks. There is always some oedema though, which is due, no doubt, to the high pressure in the capillary bed and the existence of some degree of impaired nutrition of its endothelial cells With the passage of time changes occur in the limbs of a more chronic nature.

Chronic Phase of Arterio-venous Fistula.—The compensatory mechanisms which develop in the animal or patient with an established arterio-venous fistula begin to act almost immediately after the production of the communication and are designed to restore the circulation to a more normal state To compensate for the persistent diversion of a large part of the circulating blood volume through the fistula to the detriment of other parts of the body a permanent increase in the total blood volume of the body gradually develops. This is evidenced in the first few hours by haemodilution of the blood because of recruitment of extracellular tissue fluid into the intravascular compartments. The heart rate remains permanently on the high side of normal and the cardiac output is maintained at an abnormally high level as a result of the increased venous return to the heart. The ... iented ... plays ... the chronic phase of arterio-venous fistula [41] In spite of the greatly augmented venous return to the heart the right heart pressures are not elevated nor is the high intravenous pressure at the site of the fistula transmitted to the heart but rather rapidly dissipated in the capacious venous system With few exceptions the amount of increase in cardiac output and circulating blood volume depends upon the size of the fistula and so the amount of blood being diverted,[41, 44] but on the whole the cardiac output increases more than the blood volume This diverted blood flow has been aptly referred to as the "parasitic circulation"

In response to the increased volume of blood to be circulated the heart dilates, often enormously. It has been suggested that the dilatation may be the result of decreased coronary circulation secondary to the reduced mean aortic blood pressure [31] Although in the light of our present knowledge this cannot be denied this postulate was made before the greatly increased cardiac output was appreciated The fact that the size of the heart can be restored almost to normal after closure or excision of a fistula, even a longstanding one, is proof of the preponderance of dilatation over hypertrophy of the heart. The veins on the cardiac side of the fistula undergo a similar, predominantly hydraulic, dilatation whereas the veins distal to the fistula dilate because of obstruction to the centripetal flow of blood at the level of the fistula. Thus in one case there is a volume flow dilatation while in the other there is a stasis dilatation

Once the acute phase of an arterio-venous fistula has been passed the systolic blood pressure is soon restored to normal levels. However, the persistent reduction of the peripheral resistance produced by the fistula is reflected in the diastolic phase of the blood pressure which remains permanently lowered so that an overall increase in pulse pressure becomes apparent. Accompanying these alterations in blood pressure the pulse waves show certain abnormalities. The lowered diastolic pressure means that the aortic pressure is abnormally low so that with cardiac systole there is an initial, precipitous rise of blood pressure to the systolic level. This steep upstroke produces the characteristic "water hammer pulse." Following this rapid rise of pressure the pulse falls away from the palpating finger because of the leak of blood through the fistula into the veins. The features just described, namely the increased pulse pressure, the "water hammer pulse" and the collapsing, or Corrigan, pulse, will be recognised as characteristic of free aortic regurgitation as well as of an arterio-venous fistula and depend, in both cases, upon failure to maintain an adequate diastolic pressure in the arterial tree. A final clinical observation accompanying both large arterio-venous fistulae and aortic regurgitation is capillary pulsation This may be conspicuous but since it may persist after excision of an arterio-venous fistula its mechanism is not adequately explained by the pulse pressure.[21]

In the limb the local effects of an established congenital or acquired arterio-venous fistula are, on the arterial side, mainly those of an augmented blood flow and, on the venous side distal to the fistula, those of an impaired venous return. The artery proximal to the fistula becomes thin, dilated and tortuous because of the increased blood flow through it as well as some impaired nutrition to its walls[34, 28] In some cases the vessel has become so enlarged as to resemble a true aneurysm.[34] The artery on the distal side of the fistula is usually smaller than normal but should the collateral circulation become extensively developed the retrograde flow through it to the fistula may be so large as to lead to gross dilatation of the vessel.[1] With the passage of time the arterial blood flow, which was at first greatly reduced, is restored to normal or more usually becomes greatly exaggerated The precise reason for the augmented blood flow through the collateral vessels has not been settled but it would seem to be more likely hydraulic than as a response to "tissue needs."[14] The hydraulic explanation is supported by the experimental evidence of development or persistence of collaterals even though the limb beyond the fistula is amputated. If "tissue needs" were the main reason one would not expect the blood flow to exceed the normal level The effect of this increased blood flow is observed in an elevated skin temperature which may approach the full vasodilatation level, i.e. 35°C or higher An at first puzzling finding in these limbs is that in spite of the increased arterial circulation to the limb nutritional lesions such as ulceration may develop. These are seen on the limb distal to the fistula and are due to obstruction of the venous outflow from that part of the limb which shows

all the clinical features of chronic venous insufficiency. The rapidity with which ulcers heal once the fistula is excised and the venous dynamics are restored to normal is proof of their stasis origin.

Generally speaking, the severity of the haemodynamic alterations in the body in the presence of an arterio-venous fistula, whether congenital or acquired, depend upon three factors—namely the size, the site and the duration of the fistula.[12] The first of these factors governs to a large extent the amount of blood flow through it and so governs the increased cardiac output and blood volume. The second factor too governs to a lesser extent the amount of the shunt, but an unsatisfactorily explained fact is that fistulae of equal size in the neck or upper limbs are much better tolerated than those between the vessels of the lower limbs.[25, 30] The longer that the lesion is present the greater is the strain upon the heart and cardiac failure is the eventual outcome if it is untreated. When heart failure supervenes blood volume may remain elevated but the cardiac output be within the range of normal in the presence of a large fistula—in short, the situation encountered in heart failure from any cause. In all the above respects the congenital arterio-venous fistulae have a lesser effect upon the circulation than the acquired, perhaps because the body is permitted a more gradual adaptation but more likely because the [illegible]

[illegible] in all arterio-venous fistulae, whether congenital or acquired, are the same, differing only in degree in that the general effects upon the heart and blood pressure in congenital arterio-venous fistulae are usually slight, long delayed and well tolerated for many years.

EFFECTS OF CLOSURE OF AN ARTERIO-VENOUS FISTULA

When the artery proximal to an established arterio-venous fistula is occluded temporarily certain circulatory changes develop immediately.[12, 30] The first effect of closure of the fistula is an immediate rise in blood pressure to a level in excess of the normal levels. Within a few beats the blood pressure then subsides to a level approximately that present previous to the development of the fistula. The greatest change is the restoration of the diastolic blood pressure to normal and so the pulse pressure is within normal limits. These changes are due to two factors. The restoration of the diastolic phase of blood pressure and the pulse pressure to normal levels is due to the restoration of a normal peripheral resistance when leak of blood through the fistula is prevented. The transient elevation of the systolic phase of the blood pressure is a result of temporary over-distension of the arterial system by the now inordinately excessive circulating blood volume. This latter change leads to a further cardiac dilatation which does [illegible] completely until the circulating [illegible]

hea[illegible] pressure is a reduction in the [illegible] This bradycardiac phenomenon is related directly to the altered

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Secondly, and of far greater importance to the limb, it encourages the development of an adequate collateral circulation around the fistulous site to the distal tissues, a collateral circulation without which the survival of the limb would indeed be jeopardised. Such measures are seldom used nowadays but should not be entirely forgotten.

Again, the changes discussed above may or may not be demonstrable in the patient with a congenital arterio-venous fistula. The bradycardiac phenomenon and blood pressure alterations with proximal occlusion of the involved artery are seldom pronounced. The reason for this is mainly anatomical in that it is seldom possible because of the size, number and the extent of the communicating channels to occlude them all completely.

CLINICAL FEATURES OF ARTERIO-VENOUS FISTULAE

Just as the circulatory readjustments accompanying congenital and acquired arterio-venous fistulae differ only in degree so do the clinical features of both lesions. Because of this their signs and symptoms will be discussed together but with attention to any striking differences between them Since the complaints of the patient and the signs of the condition depend, in the main, upon the haemodynamic alterations detailed above the basis for these changes will not be repeated or elaborated further

SYMPTOMS.—When the fistula has been caused by an injury the patient may recall the initial injury and demonstrate the scar in the region of which he will complain of a swelling and a buzzing noise There may be pain and tenderness locally or referred down the limb from nerves incorporated in or pressed upon by the pulsating mass. Occasionally the characteristic pain of intermittent claudication occurs and, when present, signifies an inadequate collateral circulation to the limb. Complaints may be made of swelling, heaviness and excessive heat of the limb. Varicose veins and gravitational ulcers of the lower leg must always lead the examiner to look for a congenital arterio-venous fistula when a young patient presents with such a clinical picture, particularly if it is unilateral and if the limb is excessively warm. Not infrequently the parents bring such a child saying that it is limping, the inference being that one leg is short whereas in point of fact the deformity is that of skeletal hypertrophy because of an arterio-venous fistula in the long leg and not that of post-poliomyelitic atrophy in the short (normal) one (Fig. 404). Occasionally pregnancy seems to awaken a dormant congenital arterio-venous fistula which only then becomes known to the patient. Finally the general symptoms of cardiac decompensation including palpitation, shortness of breath and even bilateral dependent oedema may lead to the mistaken diagnosis of primary heart disease while the arterio-venous fistula is either not recognised or, if recognised, not thought to be associated.

SIGNS.—The numerous signs of arterio-venous fistulae are best discussed on a regional basis.

blood pressure in that the phase of greatest cardiac slowing is simultaneous with the highest phase of arterial blood pressure. Both peak changes are fleeting and soon return to within the limits of normal. The bradycardia is reflex from the pressure receptors in the aorta and carotid arteries mediated via the vagus nerves; it can be abolished by the administration of atropine.[26, 21]

On the venous side of the circuit occlusion of the fistula is accompanied by a fall in the intravenous pressure at the site of, and distal to, the communication to more normal levels since the arterial blood pressure is no longer transmitted to them. The more important reduction in the distal venous pressure removes the effects of chronic venous insufficiency by restoring venous return from the limb to normal with rapid improvement of the trophic complications of venous stasis.

The immediate responses of the circulation to closure of the fistula are reflected in the above changes in blood pressure and pulse rate. More gradual alterations follow in that the cardiac output, stroke volume of the heart, the circulating blood volume and the size of the heart and the dilated blood vessels become restored to more normal levels. A prompt haemoconcentration can be demonstrated signifying a shift of fluid from intravascular to extravascular compartments as the first step in adjusting the circulating blood volume to the capacity of the arterial bed. It takes several weeks to restore the blood volume to normal levels. The cardiac output and stroke volume of the heart decrease *pari passu* with the reduction in circulating blood volume. The heart size probably never completely recovers, particularly if the arterio-venous fistula has been present for many years This is partly because of some permanent dilatation but also because of a small element of hypertrophy which persists although by clinical and X-ray examination the heart size is substantially reduced. A similar reduction in the size of the proximal artery and vein occurs gradually but should a true aneurysm have developed in the artery it will not recover and in some instances this has led to disaster after successful excision of the fistula.[35, 34]

The changes attending closure of an arterio-venous fistula are of some practical clinical importance when repair or excision of the established lesion is being contemplated. If any degree of cardiac decompensation exists the considerable, even though transient, increase in systemic blood pressure and the additional cardiac dilatation occurring simultaneously may precipitate acute heart failure and death. Since these changes are chiefly the result of a discrepancy between the volume content and capacity of the arterial bed which is now over-distended by a volume of blood equal to that previously being shunted through the fistula it is not unscientific to have resort to the time-honoured procedure of blood-letting to avoid acute heart strain. In preparing a patient for excision of a fistula of long duration it was customary to expose the proximal artery to preliminary periods of progressively increasing temporary occlusion. This has a two-fold benefit. First, it prepares the heart for this period of temporary strain occurring with abolition of the fistula.

normal limb. The extent of the collateral circulation can be estimated clinically in several ways. The simplest is to occlude the main artery proximal to the fistula whilst palpating the peripheral vessels. The persistence of pulses in the peripheral arteries while the main vessel is obstructed or the appearance of peripheral pulses previously absent indicates an excellent blood flow through collateral channels[34] A similar conclusion may be drawn if the blood pressure in the limb does not change or falls only slightly when the involved artery is occluded proximal to the fistula.[25]

Fig 405

Fig 404—Infra-red photograph of 28-year-old woman's legs showing prominent veins from extensive congenital arte- ... t had been diagnosed as post-polio ... ose veins of the left leg had been ... kle (Fig 405) had been unsuccess ... ng a full length one-way

Excessive length of the limb is usually a striking feature of all congenital arterio-venous fistulae but it develops in acquired lesions only if the fistula was established before epiphyseal union

The systemic manifestations of arterio-venous fistulae have already been outlined earlier in this chapter Their presence or absence depends upon the site, the size and the duration of the fistula. Generally speaking, the larger the communication and the closer it is to the heart the more severe are the effects upon the heart although exceptions have been noted.[30] An unexplained finding is that fistulae of the head, neck and upper extremities are much better tolerated than fistulae in the lower extremities and pelvis.[25, 31] Dilatation of the heart and clinical evidence of cardiac decompensation are usual findings in long-standing fistulae. The blood pressure is normal in its

The local signs in the immediate vicinity of the abnormal communication result from the fistula, the dilated artery and vein and the collateral vessels. The presence of the last may be pronounced, as often in acquired arterio-venous fistula, or they may defy localisation, as often in congenital lesions. The scar or scars of the precipitating injury is noted and a pulsating tumour is found in the course of the vessels in the region of the wound. Such a swelling may not be obvious to inspection but may be definite on palpation which will reveal the pathognomonic rough, vibratory thrill which, although continuous throughout the cardiac cycle, has a definite systolic accentuation. Auscultation will localise the characteristic bruit as maximal over the fistula but it is transmitted widely throughout the limb along the vessels above and below the site of the fistula. The bruit may be readily heard in the foot from a femoral arterio-venous communication. *In some instances when the bruit is* difficult to localise " auscultation at a distance " may be employed.[18] In this manoeuvre the index finger of one hand searches the limb whilst the examiner listens over his own forearm for the site of maximum conduction. Compression of the main artery leading to the fistula immediately abolishes the pulsation, the thrill and the bruit. The artery proximal to the fistula is usually grossly enlarged and tortuous when there is a large communication and its beat is excessively forceful. Occasionally the artery may become so degenerate that a true aneurysm results. *In congenital arterio-venous fistulae the small size* and the multiplicity of the anastomotic channels renders a palpable thrill and an audible bruit exceptional but the arterial dilatation is usually prominent and the pulse beat is forceful. The association of spider naevi and birthmarks, often extensive, and congenital arterio-venous fistulae is not fully appreciated (Fig. 403). Collateral vessels may be apparent upon examination of the region but even if not readily discernible they are manifest by the raised surface temperature of the skin around the fistula.

The regional signs are particularly evident in the limb distal to the abnormal arterio-venous communication. The most striking of these is venous dilatation in the tributaries of the major vein involved in the fistula.[27] Since the leg is the commonest site for both congenital and acquired *arterio-venous* fistulae the long saphenous system of veins is involved most frequently Varicose veins develop and may become alarmingly large and pulsate synchronously with the arterial pulse. Venous obstruction leads to the trophic changes of stasis pigmentation and ulceration (Fig. 405) The limb becomes permanently swollen from a combination of oedema, soft tissue hypertrophy and fibrous tissue hyperplasia as well as a generally increased blood volume content in the venous bed of the affected limb.

In the acute stage *the limb is usually cool and cyanotic and the major* pulses distal to the fistula may be diminished in force or absent Eventually the skin temperature becomes considerably elevated, approaching the full vasodilatation level as the collateral circulation becomes *established. The* peripheral pulses become strong and may exceed in force those of the opposite

normal limb. The extent of the collateral circulation can be estimated clinically in several ways. The simplest is to occlude the main artery proximal to the fistula whilst palpating the peripheral vessels. The persistence of pulses in the peripheral arteries while the main vessel is obstructed or the appearance of peripheral pulses previously absent indicates an excellent blood flow through collateral channels.[34] A similar conclusion may be drawn if the blood pressure in the limb does not change or falls only slightly when the involved artery is occluded proximal to the fistula.[27]

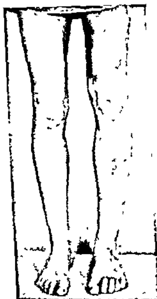




FIG. 405

Fig 404—Infra-red photograph of 28-year-old woman's legs showing prominent veins from extensive congenital arterio-venous fistulae of left leg This patient had been diagnosed as post-poliomyelitis atrophy of the right leg as a child and the varicose veins of the left leg had been excised on two occasions The stasis ulcer at her ankle (Fig 405) had been unsuccessfully excised and skin grafted She is symptom-free wearing a full-length one-way stretch elastic stocking and the ulcer is healed

Excessive length of the limb is usually a striking feature of all congenital arterio-venous fistulae but it develops in acquired lesions only if the fistula was established before epiphyseal union.

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systolic phase but an abnormally low diastolic blood pressure gives an inordinately increased pulse pressure. Further clinical evidence of the decreased peripheral resistance due to the arterio-venous leak is a "water hammer pulse" which collapses rapidly and in some cases capillary pulsation in the nail beds may be striking. A final feature of arterio-venous fistulae is the bradycardiac phenomenon usually known as Branham's sign although first described by Nicoladoni. The resting pulse rate in the patient with an arterio-venous fistula is at the upper limit of normal. When the main artery proximal to the communication is occluded the pulse rate falls to a low level while at the same time the blood pressure rises and a normal pulse pressure is restored These changes are transient but the normal pulse pressure is maintained so long as the leak is prevented since the peripheral resistance is now normal. The pulse rate soon speeds up in some degree even though the arterial occlusion is maintained but it does not reach its previous level. All of the above phenomena may be present in a congenital arterio-venous fistula but they are seldom conspicuous, since they depend chiefly upon the size of the leak and the occlusion of all the fistulous communications for their demonstration. The small size of the numerous anastomotic channels in congenital fistulae seldom permit a leak comparable to that occurring in the acquired form Also the multiplicity of the communications makes their occlusion well-nigh impossible so that blood pressure alterations and the bradycardiac phenomenon are not readily demonstrable.

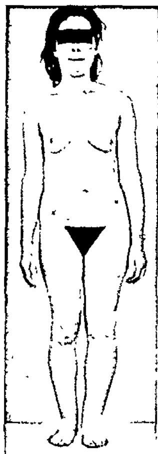


Fig. 406

Thirty-year-old woman with congenital hemi-hypertrophy of the left half of her body The left leg was 2⅜ inches longer than the right, the left arm was 2 inches longer than the right and both were greater in girth

Diagnosis.—The diagnosis of an arterio-venous fistula is rarely difficult. The thrill and bruit are pathognomonic. The history of injury is obtained in the acquired lesion and the presence of skeletal hypertrophy with varicose veins and stasis changes in a hot limb are characteristic in the congenital fistula A long hot leg is sometimes seen in chronic osteomyelitis but this can be excluded by demonstration of the old-standing bone infection which is always associated. If after a careful examination the diagnosis is still in doubt there are several aids available.

Infra-red photography may demonstrate the presence or absence of dilated veins which may not be prominent clinically and so distinguish a case of simple hemihypertrophy (Fig 406) from an arterio-venous fistula [38] Arteriography may help to localise the site of the fistula,[42] but in our experience it

has been of little value except in an occasional case of congenital arterio-venous fistula without thrill or bruit. In these patients the radio-opaque dye disappears suddenly at the level of the highest communications. Venous blood samples from dilated surface veins or by the retrograde passage of a cardiac catheter when compared to samples drawn simultaneously from the opposite limb and tested for oxygen content may confirm a suspected lesion. If multiple blood samples are taken at various levels localisation of the abnormal communication may result. Finally, plethysmography will demonstrate an augmented peripheral blood flow and when performed before and during occlusion of the proximal artery gives direct evidence of the degree of collateral circulation.

COMPLICATIONS.—Most of the possible complications attending arterio-venous fistulae have been mentioned already. In the acute stage of an acquired fistula external haemorrhage may be severe. If a large arterio-venous communication results from the injury so much blood may be diverted from the limb beyond the lesion that peripheral gangrene develops. In the established fistula varicose veins and stasis dermatitis, pigmentation and ulceration are often prominent. Should one of the dilated veins be injured bleeding from it may be alarming and difficult to control because of the increased pressure in the vein

Cardiac dilatation and congestive heart failure are frequent. Such a complication may arise very rapidly if the fistula is close to the heart and has been produced clinically when a Potts operation for the tetralogy of Fallot is performed with a fistula more than 0 5 cm. in size.

An almost unique complication of an arterio-venous fistula is a streptococcus viridans septicaemia.[17, 37A 78A] Two such cases have been reported, one between the femoral vessels and the other between the external iliac vessels, were cured by excision of the fistula The presence of a peripheral arterio-venous fistula is complicated by a high incidence of bacterial endocarditis in the heart in experimental animals but this does not seem to occur in humans

In rare cases the proximal arterial dilatation may resemble a true aneurysm and loss of the limb has followed successful excision of the fistula because of rupture of the complicating aneurysm.

TREATMENT OF ARTERIO-VENOUS FISTULA

Rarely an arterio-venous fistula may close spontaneously when the fistulous opening has been small so that fibrosis and thrombosis result.[27 33] The frequency with which experimentally produced fistulae in the vessels and in the heart will close is ample proof of this. Similarly, conservative measures such as pressure over the site of the fistula may lead to thrombosis and obliteration of the communication because of the reduced blood flow through it.[4]

Although conservative measures are seldom effective they may be the only alternative to amputation for extensive congenital arterio-venous communications in the limbs (Fig. 407, A and B). In such instances the application





FIG 407

(a) Dorsal and (b) palmar views of both hands to show an extensive congenital arterio-venous fistula involving the palmar arch and digital arteries of the right hand

of firm elastic bandages or elastic stockings, or similar rubber support if an arm is affected will reduce the tendency for the veins to dilate and will encourage the blood to flow through more normal channels while discouraging it from

entering the superficial veins and so lowering the pressure within them. It is possible too that firm elastic pressure diminishes or obliterates some of the smaller communications. Such elastic support may enable a useful limb to be retained for many years and it will, at the same time, encourage the healing of stasis ulceration, if present, or prevent its development. In the limbs amputation may be necessary because of the extensive nature alone which in some patients includes abnormal channels within the bones of the limb[39] or because of the commoner complications of extensive ulceration, recurrent haemorrhage and gangrene[28, 42] We have had to amputate only one limb in ten years for congenital arterio-venous fistulae, so that amputation is not necessary in 50 per cent of cases as has been the experience of others.[30]

In some of the smaller and more localised fistulae which cannot be excised or that have recurred after excision, particularly in the face and scalp, the injection of sclerosants as for varicose veins has been followed by cure or at least control of the lesion for some years but there is a real danger of slough of the overlying skin in these cases and the field for sclerosant therapy is not large.

When conservative measures begin to fail in congenital fistulae surgical extirpation may be attempted and occasional successes have been reported.[37, 4] The operation consists of wide exposure of the lesion and multiple ligation and division of all demonstrable communications with excision of the fistulous mass The involved artery and vein may have to be sacrificed. Very rarely a restorative procedure is possible but more usually several arteries are involved so that complete extirpation is impossible and recurrence is inevitable Repeated radical operations are usually necessary and it would appear that in some limbs the excision of one lesion or group of fistulae causes a previously dormant lesion to open up

Before and during the Second World War the surgical procedure adopted in acquired arterio-venous fistulae depended not only upon the site and the type of fistula but particularly upon the adequacy of the collateral circulation which had to maintain the distal structures when the fistula had been extirpated No operative attack was contemplated before complete assurance that the collateral circulation was sufficient to maintain the nutrition and function of the tissues distal to the fistula. Left to nature the time necessary to ensure this was from three to six months during which time the collaterals were stimulated by successively prolonged periods of proximal digital compression of the feeding artery until an adequate blood flow could be demonstrated peripherally. In selected cases or where urgency existed a preliminary or a concomitant sympathectomy was sometimes performed to produce an immediate, maximal release of collateral vascular tone and development[2] Occasionally the size and the location of the lesions was such that operation could not be delayed because of rapidly progressing cardiac decompensation The degree of acute strain being placed upon the heart by the shunt is the chief pointer to an early operation although not infrequently

an arterio-venous fistula situated in the neck or cranial cavity especially may by the noise alone necessitate early intervention to prevent serious mental breakdown.[25] With these rare exceptions, once over the acute stage of wounding an acquired arterio-venous fistula was not touched until an adequate collateral circulation around it had been ensured. The method most commonly applied was quadruple ligature with excision of the H segment which included the artery and the vein, and the fistulous track between the two[12, 25] (Fig. 401).

The ideal surgical treatment for arterio-venous fistula is resection of the fistulous track with preservation of the continuity of the artery and vein. This is seldom possible and it was for this reason that Birkham and later Matas suggested *transvenous endoaneurysmoraphy*[24] which preserves the artery at the expense of the vein. Even this reparative procedure is rarely practicable and has been followed by fusiform aneurysm at the site of repair. But with the impetus of the Korean War techniques for the collection, preservation and application of homologous artery grafts and the wider use of autogenous vein grafts have revolutionised the treatment of arterial injuries. By the early treatment of damaged arteries arterio-venous fistulae are prevented from forming, but if they do form, resection and restoration of continuity by a suitable vein or artery graft gives a high proportion of early successes in the hands of those experienced with vascular anastomoses.[43] Unfortunately long-term results are not at hand and the ultimate fate of a preserved artery in the human body is not known, though it is known that a proportion of autogenous vein grafts become aneurysmal and calcify especially if in an unsupported position in the body. It may yet be that quadruple ligation which in the past was the most frequently adopted treatment, being attended by the fewest complications and the lowest mortality rate, will return to favour. For those surgeons without the facilities for or experience with arterial grafting quadruple ligation can still be recommended.

ARTERIO-VENOUS FISTULAE IN SPECIAL SITES

There are several types of arterio-venous fistulae which merit special mention by virtue of their association with trauma or their misleading nomenclature.

"Cirsoid" aneurysm.—Often considered in the past as a tumour, a cirsoid aneurysm is really just a variant of arterio-venous fistula which has enjoyed a special name especially when occurring in the scalp. In this situation it is most frequent in the occipital and temporal areas and resembles on palpation a writhing bag of worms. Although a few may be congenital in origin the vast majority follow contusive trauma to the scalp.[7, 29, 33] It is probable that the majority of so-called congenital ones originated in birth injuries In some instances a pre-existent congenital naevus or angioma has been the starting point with injury as the precipitating factor. The term "cirsoid" is generally applied when the contributing arteries and veins form multiple

ıications so that a diffuse arterio-venous fistula arises (Fig. 408). Occa- such fistulae in the scalp have connections with intracranial vessels. ̈ırsoid" aneurysms demonstrate all the local and regional effects of venous fistulae but are seldom complicated by the systemic cardio- r effects Surgical extirpation is the procedure of choice in the treat- f such lesions An advisable pre- y step is ligation and division of incipal artery or arteries leading fistulae[7] If on the scalp a full- ess haemostatic flap can then be down[29] The fistulae are in this hich is then dissected free of com- ations and once completely cleared laced Should surgical excision be ctical or unsuccessful a combination rgery and multiple injections with ısing agents has been attended by success



Fig. 408
Buttock of a 28-year-old man who was kicked in the buttock at the age of 12 years. The arteriogram of this "cirsoid" aneurysm is shown in Fig 176

'ulsating exophthalmos.[12 15 23]—When ıbnormal communication becomes ılished between the internal carotid y and the cavernous sinus pulsating ıhthalmos occurs associated with the acteristic intracranial thrill and bruit ribed by patients as "buzz like a " "hum like a top," etc The bruit is capable and may become almost un- rable to the patient. It is best heard r the eyeball and, with the thrill, can be modified or eliminated by com- ssion of the common carotid artery in the neck. The bulging eyeball sates in time with the heart beat There may be alarming subconjunctival emorrhage, oedema of the lids and even of the forehead, particularly when origin has been traumatic. Sometimes loss of sensation in the skin 'as innervated by the first and second branches of the fifth nerve occurs well as ophthalmoplegia from compression of the third, fourth and sixth rves in the confined space of the cavernous sinus Although this picture ay be found with vascular tumours of the orbit and simple aneurysms of e internal carotid and ophthalmic arteries these lesions are usually easily stinguishable from the pulsating exophthalmos of an arterio-venous fistula etween carotid artery and cavernous sinus

In 75 per cent of cases of communication between the ... rtery and the ... he base of ... ıus sinus a...

may be torn with the immediate development of all the features of a fistula. In some cases the vessel wall is injured and gives way later so that the signs and symptoms are delayed in onset. The traumatic type is most common in men of about thirty years of age whereas the spontaneous type of fistula which makes up the remaining 25 per cent. is most frequent in women of about fifty years of age. In this group hypertension is common but there is no direct history of trauma, and atherosclerosis and syphilis do not seem to be factors in their development.

The condition was first recognised by Travers in 1809 and he suggested and performed ligation of the common carotid artery in the neck. This procedure alone will cure about two-thirds of all cases. Whatever measure is adopted it must be preceded by progressively increasing periods of daily digital compression of the common carotid artery in the neck until no evidence of headache or motor or sensory signs on the opposite side of the body develop after a period of at least thirty minutes compression. Approximately 25 per cent. of lesions will be cured by compression alone,[23] and a number of small fistulae heal spontaneously by thrombosis or fibrous contraction of the abnormal communication.[31] In the remainder ligation of the common carotid artery or preferably the internal carotid artery will be necessary for cure. The purpose of such procedures is to reduce the amount of blood going to the arterio-venous fistula without diminishing the blood supply to that side of the brain sufficiently to cause death or hemiplegia. If thirty-minute periods of digital compression done at least ten times per day abolish the bruit and are not accompanied by neurological signs on the opposite side of the body carotid artery ligation is indicated. This is performed under local anaesthetic and the internal carotid artery is temporarily clamped for thirty to forty-five minutes. If followed by no ill effects it is permanently ligated. This will result in about 90 per cent. cure and is the procedure of choice. If ill effects follow its ligation the temporary ligature must be removed and in these cases the common carotid artery may be ligated with a high proportion of cures and great amelioration of symptoms in the remainder.

R. B. L.

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CHAPTER XXVII

TUMOURS OF BLOOD VESSELS

1. ANGIOMA

RIBBERT'S theory that haemangiomas develop as a proliferation of th embryonic vascular network is still generally held, and is supporte by their congenital incidence. There is no present explanation of thei greater frequency in the female sex. They can be classified as capillary o cavernous. *All varieties may ulcerate or may induce hyperkeratosis in th* overlying stratum corneum. Malignant forms occur, and perhaps the con genital *cirsoid aneurysm should be included here also.*



FIG 409
Capillary angioma (strawberry tumour) on the outer side of an infant's leg.

The capillary haemangiomas.—These include two-thirds of all vascular tumours. They include the cutaneous naevus, the telangiectasis, the "port-wine" stain and the "spider" naevus.

The cutaneous naevus, capillary haemangioma of skin, haemangioma simplex, or salmon patch (Fig 409) is a pink or red network of small capillaries without much cellular proliferation, radiating from a central "punctum" which is an artery of the subcutis supplying the tumour.[1] This tumour lies flush with the surface unless associated with epidermal proliferation. It may occur on any skin surface, but is commonest on the face. It may be multiple and there is great variation in size. Usually it is strictly unilateral and, even when extensive, *it rarely transgresses the median plane. A similar tumour may* occur on mucous membrane In the central nervous system a capillary

angioma is usually a small, red, spongy tumour embedded in the wall of a cyst.[2]

The strawberry patch (Fig. 410), also a capillary haemangioma, is bright red, lobulated and raised above the surface, often growing rapidly with "outsider" extensions at first separate from it but later fusing with it; this variety very commonly ulcerates.

The telangiectasis is a dilatation of normal capillaries rather than a disturbance of vascular development. The spider naevus or naevus araneus is of this character; it develops in the skin of the face in adult life, often in patients with liver insufficiency, the naevus fading with intermissions and returning with remissions of the liver disease. It may also develop during pregnancy and it arises sometimes in males in association with gynaecomastia, which is sometimes also a sign of liver disorder.[3] The spider naevus persists on elevation of the arm, but disappears at death, emptying when the other small arteries empty. Multiple congenital telangiectasis (Osler's disease)[1] is a familial disease inherited as a Mendelian dominant, with often a skip of a generation; tiny capillary haemangiomas are scattered over mucous surfaces and sometimes skin as well and may give rise to unexplained haemorrhage, gastro-intestinal for example, or insidious anaemia

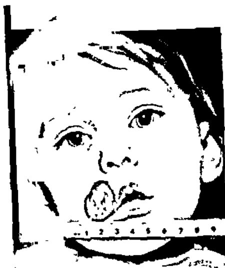


FIG 410
Capillary angioma (strawberry tumour) of upper lip.

The de Morgan spot or naevus flammeus (Fig. 411) is a uniformly red capillary naevus a couple of mm in diameter without a central arteriole. It develops in middle age, mainly on the trunk Its age incidence has wrongly given rise to a suspected correlation with cancer.

Port-wine stain or naevus vinosus (Fig 412) is a pink, blue or purple haemangioma of the skin, a generalised telangiectasis of the capillaries usually on the face but sometimes involving also lip or buccal mucosa

The ...

... it a ...

naevus, ... is desired for it, can be coagulated by touching the central punctum with a diathermy needle. The port-wine stain is perhaps



Fig. 411
Campbell - de Morgan spots



Fig 412
Capillary haemangioma (port wine) in territory of ophthalmic division of trigeminal nerve

st left untreated, to be camouflaged with specially prepared powder, though cellent results have been obtained by irradiation of dark violet stains. An abrasive" treatment has also been described[4]; after infiltration with ocaine-adrenaline to produce a firm cushion, the affected area is sand-



FIG. 413
Sclerosing angioma of back

apered into but not beyond the cutis, bleeding being controlled by wet gauze ressure. The best results are obtained if the colour of the naevus is red with tinge of blue. A nearly normal colour may also be obtained in the affected rea by tattooing with various metallic oxides and sulphides blended by trial nd error to give normal complexion Conway's papers[5] should be studied or preparation of the palette.

The subcutaneous naevus may be covered by healthy skin, or the overlying kin may be included in the haemangioma (mixed naevus). It presents as a luish, spongy tumour, composed of dilated capillaries, but the capillary hannels are frequently compressed by diffuse endothelial proliferation, ufficient sometimes to justify the title "angioblastoma." The purely sub-utaneous variety shows a pronounced tendency to fibrosis, shrinkage and

spontaneous cure (Fig. 413) but this tendency should not be relied upon. The results of the Chaul X-ray unit for deep lesions, or the Philips unit for small lesions on the face, are excellent, and both these methods can safely be applied when the child is first seen, however young.[6] Irradiation gives results more satisfactory usually than electro-coagulations. The mixed naevus exhibits little tendency to spontaneous cure, unless ulceration and infection occur in it.



FIG. 414
Cavernous haemangioma of lip.

If its site or size render excision undesirable, it should be treated by radium plaque rather than by carbon-dioxide snow or electro-coagulation.

The cavernous haemangioma.—This occurs in the subcutaneous tissue of skin or mucous surfaces (Fig. 414) as a bluish elevated plaque; in the liver it presents a firm blue mass, and it may occur in similar form in any of the internal organs. The tumour is composed of dilated blood spaces with thin walls, supported by a tenuous stroma. In rare cases the cavernous angioma is pulsatile, as a result of an acquired communication with a large artery. The tumour rarely coagulates spontaneously, organising and even calcifying as a hard nodule, but most require excision with some form of plastic repair if a wide area of skin is involved.

The sclerosing angioma[7] produces a non-melanotic pigmented tumour of the skin. Its relationship with histiocytoma is disputed. There may be a history of a congenital slow-growing naevus becoming quiescent and then enlarging in size with deepening pigmentation, very similar except for



FIG 415

Diffuse haemangioma of hand

its quiescent period to a malignant *melanoma* as it supervenes on a benign pigmented tumour Usually solitary, *the* sclerosing angioma may be blue, violet, purple brown, red, light *brown*, pink, or yellow in colour Most of them are on limbs [illegible]
angiom[illegible]
with a [illegible]
tissue which may mask other elements. [illegible] of both. There is also dense fibrous histiocytomas may *do*, after inadequate removal.

A diffuse angioma of the deeper tissues [illegible]
affect [illegible]

2. ANGIOSARCOMA

Angiosarcoma[9] affects equally males and females, most often of Italian or Jewish race, and young people and children are the usual victims. It is commonest in the extremities (Fig. 416) and affects soft parts rather than skin. Growth is rapid and it becomes a bulky, painful tumour liable to haemorrhage. A special form affects the nasal cavity. Death is usually from lung involvement. Angiosarcoma is radiosensitive but a guarantee of cure can only be given in



FIG. 416
Diffuse haemangiosarcoma of left upper extremity

the case of an angiosarcoma of an extremity or of the breast treated by radical amputation. A special variety of angiosarcoma (haemangio-endothelioma) occurs in bone,[10] sometimes with involvement of internal organs such as spleen.[11]

Angiomas of solid, proliferative type may, after trauma, or spontaneously, increase suddenly in size, and even metastasize widely. This rare malignant change, which occurs only in adult life, is sufficient reason for the removal of any angioma which exhibits a sudden increase in size. A primary angiosarcoma occurs in the infant liver, giving hepatic enlargement and ascites soon after birth, and sometimes replacing the liver entirely by a large angioma of

cavernous type, with solid, malignant, endothelial masses scattered through it. One unique case of an angiosarcoma of a limb the seat of chronic oedema, was haemangiosarcomatous

3. KAPOSI'S MULTIPLE HAEMANGIO-SARCOMA[12]

Kaposi's disease (Fig. 417) appears to be a vascular tumour allied to the angiosarcomas.[13] The disease affects predominantly male Jews and Italians over forty years of age, though it has been described even in teen-age males of

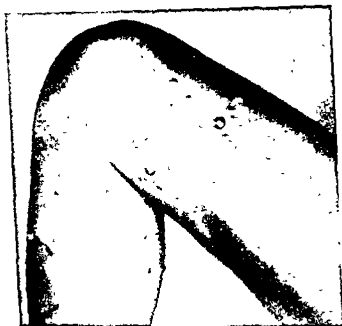


Fig. 417
Angiosarcoma of Kaposi. (Dr Van Wyk's case)

these races. The disease is also common among the Bantus of South Africa and it occurs in American negroes. In most cases it begins in the skin of the lower, or less commonly upper extremity, though it may start in the penis or even primarily in the internal organs In many patients the initial lesions develops in legs the site of chronic oedema A bluish-red demarcated macule appears, rather like a melanoma The macule grows and becomes more elevated and other macules appear near it and fuse with it The other extremity often suffers too, and the disease spreads like more or less symmetrical stockings to the trunk It is painless except for the nodules on the penis or soles of the feet The internal organs ultimately suffer too, and rarely the disease may start in the heart, kidney, liver, intestines, lymph-nodes, eye, ear or pharynx. Histologically the early macule looks like an angioma with haemorrhages; later there is endothelial and fibroblast proliferation, and finally the

sarcomatous pattern is obvious. Most pathologists regard this as an angiosarcoma, though some place it among the reticuloses.[14] The disease in the skin may be controlled by radiotherapy and patients can be kept going with repeated doses over a long period of years.

4. GLOMUS TUMOUR. ANGIOMYONEUROMA

This small painful tumour[15] was described by Wood in 1829,[16] but was familiar to English and Continental writers before him. In our own

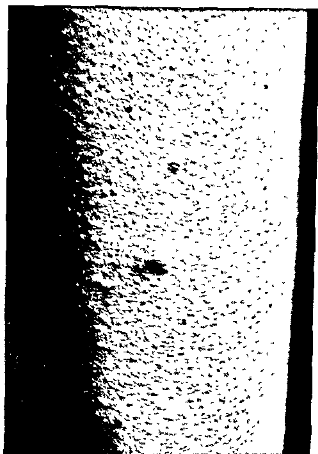


FIG. 418
Glomus of front of leg; pigmented areas are concomitant benign moles

generation, Barre[17] clearly described a bluish subungual tumour producing paroxysms of pain radiating up the arm to the neck and right side of the trunk, associated with Horner's syndrome and changes in the vasomotor reflexes, and relieved by excision of the tumour; later, with Masson[18, 19, 20] he related the tumour to the normal arterio-venous anastomoses of the distal extremities. This relationship was also remarked by others.[21, 22]

Direct communications between the arteries and cavernous sinuses of the penis were first observed in 1844 by Muller, who later described similar

direct arterio-venous communications in various parts of the human body. The subject was well reviewed by Clark in 1938.[23] Grant (1930)[24] studied the A.V. anastomoses of the living rabbit ear. He observed that when the ear was warmed, the arteries dilated at 35°C., and the A.V. anastomoses opened at 40°C. He found the communications very numerous in this situation—25 to 50 per sq. cm.—and concluded that they were important in maintaining body temperature. When dilated, the communications short-circuited the capillaries.



FIG. 419.
Subungual glomus tumour

The glomus tumour lies in the corium, but may grow in depth to fill the subcutaneous space over the area of its extent. Its greatest diameter is seldom of more th... Th... cm. tur... the

Histologically[25] the tumour presents a tangled mass of blood vessels lined by a layer of flattened or swollen endothelial cells on a supporting ... stroma and ... either ... epithel... glomus cells, which have well-defined outlines often accentuated by intercellular collagen, may have short contractile fibrils within their cytoplasm; they may lie inside, or outside, or on both

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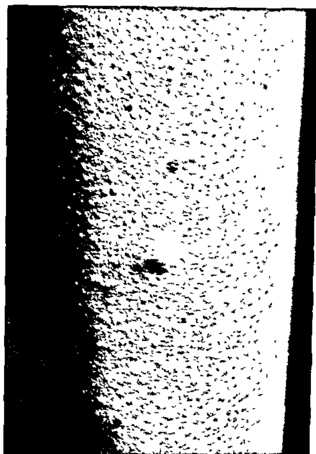


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Other symptoms observed have been flushing and warmth of the affected extremity, attacks of pallor, coldness and sweating, and under-development of the affected part.

The PHYSICAL SIGNS depend upon the location, size and depth of the tumour, but local tenderness is constant. Most glomus tumours are blue or purplish; only a few are red; the colour may change, or vary in intensity, with alterations in the position of the limb or compression of feeding and draining vessels. The colour of a subungual tumour may not be detected through the nail. Only the most superficial tumours are palpable, but the overlying skin of cutaneous or subcutaneous forms is often wrinkled, thin and damp with hyperidrosis, the overlying nail of subungual varieties unduly convex, thickened and longitudinally striated from retardation of its growth. Underlying bone may be eroded, excavated or rarefied; in two cases the tumour seems to have been situated within the actual bone of a terminal phalanx.[35, 36] The affected extremity is usually warmer than its fellow of the opposite side. Oscillometry may show 100 per cent. increase in arterial excursion, and by the plethysmograph method the flow in the limb may be shown to be extravagantly increased.

During an attack of pain, vasomotor changes may involve the entire extremity, which may pale, cool and sweat, and a unilateral Horner's syndrome may be observed; the pain is sometimes, in fact, associated with extreme local sympathetic overaction.

The TREATMENT of glomus tumour is surgical excision; the cutaneous and ungual changes may persist after operation, but pain, tenderness and vasospastic attacks are relieved.

I. A.

aspects of the muscular layer of the vessel wall, and in glomus tumours there are both myelinated and non-myelinated fibres in relation to the glomus cells; normal A.V. communications have only non-myelinated fibres in relation to them. Masson recognises four types of glomus tumour: (1) predominantly angiomatous; (2) with fewer vessels and more musculo-endothelial stroma; (3) neuromatous; and (4) degenerative, with a generous hyaline and mucoid interstitium. Probably in this group also should be placed the "haemangiopericytoma" of Stout and Murray,[26] a rare tumour rather like a glomus tumour, but without painful or vascular effects, varying greatly in its behaviour but sometimes malignant.[27] The myoma of skin which usually seems to arise from blood-vessel muscle[28] may closely mimic glomus tumour in its behaviour, and should perhaps be grouped in Masson's second category. The cutaneous myoma arising in the erectores pilorum gives a larger painless tumour usually mistaken for a fibroma.

Clinical features.—Most glomus tumours (Fig. 418) have occurred in the extremities, two-thirds of them in the upper limb, though an occasional tumour occurs on the trunk. One-half are digital and one-third subungual (Fig. 419). Females suffer most from glomus tumours of fingers and toes, males from tumours more centrally situated.[29] The youngest patient was two weeks old[30] and the oldest forty-three years,[31] but most seek treatment in the twenties. The duration has varied inversely as the degree of pain. Pain is absent in less than 2 per cent., and even this minority has superficial tenderness at the site of the tumour The pain may be exquisite, agonising, burning, throbbing or bursting in character, and occurs typically in paroxysms which are induced by pressure, heat or cold, or arise spontaneously. Relief may be sought by the application of cold or heat, and a bandage or a glove may be worn continuously for protection. Pain following trauma may attract attention to the tumour, or trauma may incite pain in a previously painless tumour. The pain may be sharply localised, or so diffuse that the tiny trigger-spot is not located. If the tumour is subungual, the patient may leave the overlying nail uncut and unfiled. Sudden trauma to the tumour may make the patient faint Some tumours, emptied by slow pressure, may remain colourless and painless for hours.[32] The pain may seem so grossly disproportionate to the size of the tumour that a psychoneurosis is blamed for it. The cause of the pain is obscure; a similar pain may occur in congenital A.V. fistula even without the presence of a glomus tumour,[33] and can sometimes be sharply localised by stroking the skin of the affected area with a pinhead.[34] Changes in the blood pressure may influence the pain; it may be relieved by elevation and be increased by dependency or by the application of a sphygmomanometer cuff If the veins of the affected extremity are emptied by elevation, and a sphygmomanometer cuff rapidly inflated then to a pressure higher than systolic, relief may be prolonged. The paths followed by glomus tumour pain are not known; simultaneous block of both sensory nerves and sympathetic chain may fail to abolish the pain, or may merely change its character.

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CHAPTER XXVIII

GANGRENE

"The important feature of gangrenous tissue is that it is dead and therefore useless, for there are no degrees of deadness" (Learmonth).[3]

GANGRENE is the term applied when there is death of a part of the body from deprivation of its blood supply. The death of tissue may be pure ischaemic necrosis without putrefaction—dry gangrene, or it may be accompanied by putrefaction or decomposition of the affected tissue—wet gangrene. Whether gangrene is wet or dry depends largely upon three factors. first, the amount of water in the limb when blood flow ceases; secondly, the rate at which the tissues subsequently lose moisture; and thirdly, the presence or absence of infection. Thus dry gangrene is more likely to develop in a limb slowly deprived of its circulation and in a part that has a large surface area relative to its volume. Wet gangrene is usual when there is abrupt cessation of blood flow to a large portion of a limb which is the seat of venous stasis or oedema or when gangrene supervenes in inflamed tissues. Whether gangrene is wet or dry, however, helps very little in determining the cause of the deprivation of blood supply and there is little virtue in retaining the terms in more than a descriptive capacity.

Although by the time gangrene is present gross disease of a major vessel is usually evident it is too little realised that the fate of a limb is sealed in the capillary bed The tissues of the body depend upon an adequate supply of blood for their nutrition The large arteries and veins are merely conduits carrying blood to and conducting it from the capillary beds which contain only about 5 per cent of the circulating blood volume Thus obstruction or narrowing of the conducting systems may reduce capillary blood flow to a level incompatible with life Alternatively, any interference with blood flow or vascular exchange in the capillary bed will lead, if it is sufficiently severe, to death of a part of a limb These considerations have led Learmonth[3] to classify gangrene in three major groups:

1. **Lesions of the efferent pathways**—arterial diseases.
2. **Lesions of the afferent pathways**—venous diseases.
3. **Lesions of the effective apparatus**—diseases of the capillary bed

By far the largest group is narrowing or obliteration of the major arteries to a limb, and the major cause is atherosclerosis. Gangrene resulting from venous obstruction is rare because of the extensive alternative pathways which exist in the venous system. Primary interference with vascular exchange in the capillary bed is not a frequent cause of gangrene but does occur in

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may be completely severed or severely lacerated and in such circumstances the extent or even the development of gangrene depends largely upon the behaviour of the collateral blood vessels. If there is an extensive periarterial haematoma they may be mechanically compressed but more usually there is a greater or lesser degree of collateral vasospasm and this, with the collateral-forming potentialities of the region concerned, influences the extent or development of gangrene. Less frequently gangrene may follow indirect trauma in which the major artery to the part is not openly or directly injured. Thus injury to nearby tissues may cause severe arterial spasm which if not relieved may lead to death of tissue. Gangrene has been recorded after indirect trauma to the subclavian artery by a cervical rib and to the axillary artery by long continued crutch pressure. Loss of a limb has occasionally followed injudicious application of a tourniquet and, fortunately rarely, following the application of a plaster of Paris cast In the latter case gangrene is predominantly the result of interference with venous circulation. In peace time gangrene of a limb after trauma is uncommon and when it does occur is usually the result of industrial and road accidents.

Infection.—Specific infections which may be followed by peripheral gangrene are mainly *syphilis* and *gas gangrene*. In civilian practice gas gangrene of the limbs is rare. We have seen only two cases in 200 patients with gangrene—one of these followed extensive trauma to an arm and the other complicated a pelvic abscess which had developed around a ruptured diverticulitis and led to gas gangrene of the leg. Gas gangrene of a limb has followed the application of plaster of Paris and the use of catgut contaminated with the clostridium group of organisms.

The exact rôle of syphilis in the development of acral gangrene is hard to assess and if it does occur syphilitic gangrene is a rare event indeed. Leriche,[6] whose experience of peripheral vascular disease is almost unparalleled, has never seen a case of gangrene attributable to syphilis alone. It is said to occur as a bilaterally symmetrical digital gangrene in the newborn congenital syphilitic and again in the middle-aged tertiary luetic. We have never seen a case of either.

Non-specific infection leading to loss of a limb or a part of it has fallen into two categories in our experience. First, loss of a digit or usually the terminal phalanx following a complicated pulp space infection, and secondly, post-operative synergistic spreading gangrene of the skin.[11] Non-specific spreading *infection* is a common reason for amputation of an arterially deficient extremity but as a primary cause of gangrene in a limb with a normal circulation it is very rare.

Physical causes of gangrene include the destructive effects of heat, cold, chemicals and electricity upon the peripheral circulation (*see* Chapter XV). Of these the effects of cold in the form of frostbite and immersion foot are the most frequently encountered but superficial gangrene has followed haemagglutination of red cells from cold in susceptible individuals. Rarely

conditions such as frostbite and cold haemagglutination. In the final analysis, however, it is failure of the capillary bed to supply oxygenated blood to and remove metabolites from the tissues which causes gangrene in a limb.

In a recent review of 200 cases of gangrene of the extremities and from a review of the literature Lynn and Modlin[10] have developed the following classification which will enable the reader to remember most of the causes of gangrene. It is apparent from this list that the vast majority of cases of gangrene are due to disruption of the afferent pathways. Most of the conditions have been discussed elsewhere in this book and the reader is referred to the relevant chapters for details. Only those causes not covered previously will be elaborated.

CAUSES OF GANGRENE

Trauma	Direct Indirect
Infection	Specific Non-specific
Physical	Heat Cold Chemicals Electricity Radium and deep X-rays

Symptomatic—

- Thromboangiitis obliterans
- Raynaud's " disease " and " Collagen diseases "
- Embolism
- Atherosclerosis
- Thrombosis — Arterial; Venous
- Metabolic—diabetic atherosclerosis
- Ergot
- Neonatal
- Trophic

Trauma (*see* Chapter XV).—Gangrene of a limb may follow direct injury to its major artery by a bullet, knife or other form of trauma. The artery

found in a younger patient, is more likely to be infected, is commoner in women than men and is more often capable of treatment by medical measures or conservative amputations.[1]

Ergot poisoning is a rare cause of acral gangrene. It usually develops in the limbs days or weeks after infected rye bread has been eaten. Reports of gangrene after the use of ergotamine preparations in the treatment of migraine and the pruritus of jaundice have been recorded.[4] The essential lesion in ergot gangrene is arterial thrombosis secondary to unremitting arterial spasm. Ergot preparations should be used with great care when there is peripheral vascular disease present or in the presence of digital infection. Ergotism nowadays has little practical importance.

Neonatal gangrene develops in infants within a few days of birth and is usually symmetrical, involving the digits of both upper or lower limbs. The etiology is unknown. One case we saw progressed to gangrene of both legs and here it may be possible to postulate uncontrolled thrombosis extending from the natural obliteration of the umbilical arteries. The last infant seen had a localised gangrene of one foot and suffered from galactosuria. Neonatal gangrene is rare.[12]

Trophic causes of gangrene are usually the result of infection developing in an ulcerated limb the seat of a neuropathy as in diabetes, syringomyelia, tabes dorsalis or leprosy. It is not common.

THE PREVENTION OF GANGRENE

Since more than 90 per cent. of gangrene of the extremities is due to obliterative vascular disease there is usually clinical evidence of an impaired circulation prior to the development of overt gangrene. The history and examination may reveal intermittent claudication, abnormal coldness, colour changes, absent or deficient arterial pulses, nutritional changes or rest pain. The peripheral circulation may be very poor but still compensated so that it is the duty of the clinician to prevent a breakdown. It is unfortunate that the beginning of gangrene is not heralded by dramatic pain; if it were the end results would doubtless be very much better and fewer people would be treated for fallen arches and rheumatism while circulatory compensation in their limbs fails. The prevention of gangrene in a limb may be discussed under two headings: first, the avoidance of factors which may precipitate gangrene, and secondly, the development of the collateral circulation.

Avoidance of precipitating factors.—The conditions usually responsible for a breakdown in circulatory compensation in an ischaemic limb are trauma, infection and temperature changes. Usually one follows the other as a blister from an ill-fitting shoe becoming infected or infection developing in a toe following careless paring of the toe nails or a corn. The effect of such conditions is to increase the demands of the tissues beyond the ability of the circulation to supply them and death of tissue results. The simplest way of preventing the d...

a deep third-degree burn may involve a major artery with gangrene of the limb. Similarly, a deep electrical burn may char an artery or so damage it that extensive thrombosis and gangrene ensue. Damage to a limb or its actual loss from the injudicious application of radium needles or deep X-ray therapy is exceedingly rare now.

Chemicals such as strong acids and alkalis may cause gangrene of a digit or a limb. The most frequent chemical in the past was pure carbolic and the digits of nurses often suffered. Gangrene of a digit has followed the extravascular injection of local anaesthetic particularly when a tourniquet was applied as well.[2] There are a number of substances which if injected intra-arterially will cause extensive spasm, thrombosis and gangrene. The better known of these are sclerosants accidentally injected intra-arterially in the treatment of varicose veins and pentothal (thiopentone) injected into an abnormally superficial ulnar artery at the antecubital fossa during the induction of anaesthesia.

Thromboangiitis obliterans[7] (*see* Chapter XI).—Buerger's disease is second only to atherosclerosis as a cause of gangrene in peripheral vascular disease but it is the commonest cause of gangrene of the upper extremities

Raynaud's "disease" (*see* Chapter XIV.)—Gangrene of the digits never occurs in Raynaud's "disease" in the absence of thrombosis of the digital arteries of the affected fingers.[9]

Embolism (*see* Chapter XII) —Embolic obstruction to the flow of blood through a major artery is usually caused by a blood clot detached from the fibrillating left heart in chronic rheumatic heart disease. Smaller emboli may become detached from the valve cusps in bacterial endocarditis and from plaques of atheroma. Arterial embolism by tumour masses has been reported but is exceedingly rare. The femoral artery is the site of obstruction in almost two-thirds of cases.

Atherosclerosis (*see* Chapter IX).—This is the commonest cause of gangrene in peripheral vascular disease. The lower extremities are primarily affected.

Thrombosis (*see* Chapter IX) —Acute arterial thrombosis which leads to gangrene of a limb may simulate arterial embolism very closely but the older age of the patient, the absence of fibrillation and, in most, a previous history of deficient arterial circulation help to differentiate the two. Arterial thrombosis occasionally develops as a complication of dehydration and toxicity in such diseases as typhoid and typhus fever and, for less clear reasons, during the convalescence from pneumonia.

Venous thrombosis sufficiently extensive to cause peripheral gangrene is only found in the condition known as phlegmasia caerulea dolens.[3] This massive venous thrombosis is usually complicated by a greater or lesser degree of arterial spasm (*see* Chapter XXI).

Metabolic gangrene is a term used only to separate diabetic atherosclerosis from the more usual senile atherosclerosis. Diabetic atherosclerosis is usually

are no constitutional effects and no cellulitis. Rest pain is an ominous symptom. If there is doubt conservative measures such as bed rest, control of infection by systemic antibiotics and mild local antiseptic baths to the part and control of diabetes should be instituted. Gangrene caused by frostbite, immersion foot, phlegmasia caerulea dolens and plaster of Paris compression is seldom more than superficial and must always be treated conservatively for as long as is practicable. In the last condition an arteriogram may be decisive in planning treatment, and in avoiding major amputation.

When a limb or part of it has been amputated the patient must be rehabilitated as soon as possible. This is particularly important in the older patient who must be got up as soon as possible with a temporary prosthesis (pylon) until the stump is ready for the final artificial limb. The old attitude towards elderly amputees is seldom encountered now and it is rare indeed for the Limb Centre at Rochampton to fail to rehabilitate them.

R. B. L.

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conscious." Protection of the feet from trauma and extremes of temperature is paramount. Well-fitting shoes and warm wool socks must be worn. At night bed socks should be worn and hot-water bottles avoided. Great care must be exercised in cutting the toe nails, corns or blisters. The feet should be washed daily in tepid water, carefully dried with a soft towel and kept dry by the daily application of spirit and powder, paying particular attention to between the toes. By such measures a poor but still compensated peripheral circulation can be protected from breakdown.

Development of the collateral circulation.—The best method of achieving maximal development of the collateral circulation in an ischaemic limb is *by performing cervico-dorsal or lumbar sympathectomy. Vasodilating drugs* are not beneficial[6] and the benefit of active and passive vascular exercises and the oscillating bed is difficult to assess. We do not advocate them in any *form Valuable medical measures include the provision of proper rest and* deep sleep. Anaemia and dehydration are corrected. Reflex heating may be employed, abstention is advised from tobacco. Alcohol is a good vasodilator and we recommend its use in moderate doses, especially as a night cap to encourage sleep and the dilatation of the peripheral circulation which accompanies it. Sympathetic denervation in selected cases improves the collateral circulation and so the limb nutrition, and should amputation become necessary less radical procedures may be possible.[7] The surgeon dealing with peripheral vascular disease should remember the dictum ascribed to Finney that *"anybody can amputate a leg, but it takes a good surgeon to save one."* Thus all one's efforts should be directed towards the prevention of gangrene in a limb by *educating the patient in the care of his feet and encouraging the development* of a good collateral circulation. More specific measures for particular forms of gangrene—arterial trauma, embolism, atherosclerosis, thromboangiitis—are discussed elsewhere.

TREATMENT OF GANGRENE

Once gangrene is established amputation in some form is inevitable. The important thing is to conserve as much of the limb as is possible and practicable to its function. In short, amputation must be performed at as high a level as is necessary but at as low a level as is possible.

Rarely amputation is performed as a life-saving procedure in overwhelm*ing infection or spreading gangrene.* More usually amputation is an elective procedure to remove gangrenous, and therefore useless, tissue The level of amputation is also influenced by the types of prosthesis available. The best *sites for amputation are disarticulation of toes through the* metatarsophalangeal joint, the transmetatarsal plane, the upper third of the leg, the knee, and the lower third of the thigh. The techniques of these operations are discussed in Chapter XXIV.

Conservatism is justified in all cases but especially when gangrene is limited to one toe, is well demarcated and not spreading, and when there

and third ganglia removes those nerves arising from the second and third thoracic segments and also interrupts the fibres ascending from the thoracic segments below the level of the third, thus abolishing the clinically important supply to the upper limb.

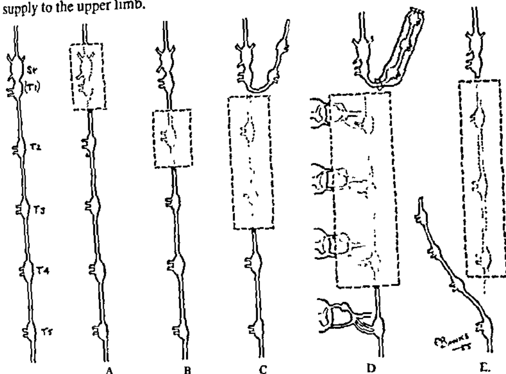


FIG 420

Operations for sympathetic denervation of the upper limb.
A Removal of stellate ganglion B. Operation of Goetz C. Operation of Telford
D Operation of Smithwick E. Operation of Haxton

Telford[7] suggested division of the sympathetic chain below the level of the third ganglion, and division of the grey and white rami connecting the second and third ganglia to the intercostal nerves, only preganglionic nerves thus being divided (Fig 420D). Smithwick[8] in order to prevent regeneration suggested division of the sympathetic trunk below the level of the fourth ganglion with intraspinal section of the second and third and fourth thoracic nerve roots, preferably intrathecally, and in addition capping of the upper end with a silk sleeve (Fig 420E)

3 EXCISION OF THE SECOND THORACIC GANGLION ALONE.—This has been suggested[5] (Fig 420B) but recurrence of symptoms would appear to be more rapid after this as the distance over which regenerating fibres would have to travel is small. This limited operation is not recommended

Recurrence of some sympathetic activity in an upper limb after operation occurs in the majority of cases after an interval of six to twelve

CHAPTER XXIX

THE OPERATIVE SURGERY OF THE PERIPHERAL VESSELS

SYMPATHECTOMY

THE sympathetic nerves to the peripheral vessels are carried in the somatic nerves, from which they pass to the peripheral arteries at successive levels in the limb. Local anaesthesia of the main nerves to the limb leads to maximum dilatation in the territory supplied by the nerves. There is, therefore, no place for periarterial sympathectomy of the vessels at the roots of the limbs.

CERVICAL SYMPATHECTOMY

The preganglionic sympathetic fibres supplying the upper limb emerge from the first to the tenth segments of the spinal cord. They ascend in the paravertebral ganglionated chain to relay largely in the stellate ganglion, but also to a lesser extent in the middle cervical ganglion, the second and even the third thoracic ganglia [1,2] The extent of the contribution from the first thoracic ganglion seems to vary in degree, and some consider it significant, but in a series of seventeen patients examined by one of us (p 117), patients who had undergone removal of the second and third ganglia only, leaving the first ganglion intact, there was no evidence of remaining sympathetic function in the hand. Haxton,[3] after a series of carefully conducted experiments, concluded there was some sympathetic outflow to the hand from the second and third thoracic segments, although this was often of little clinical importance, and that there was an occasional, usually insignificant, contribution from the first thoracic segment.

Sympathetic nerves destined for the upper limb can therefore be interrupted by:—

1. EXCISION OF THE CERVICOTHORACIC (STELLATE) GANGLION.—Not only will the upper limb be almost completely sympathectomised by this operation, but also the ipsilateral side of the head and neck. If there is a significant contribution from the second and third thoracic segments through communications from these to the brachial plexus, without passing through the cervico thoracic ganglion, then denervation of the hand will be incomplete (Fig 420A)

2. EXCISION OF THE SECOND AND THIRD (AND FOURTH) THORACIC GANGLION As the first thoracic segment is responsible for the sympathetic supply to the head and neck, and as its contribution to the upper limb is insignificant,[4,5,6] removal of the first thoracic ganglion is best avoided Excision of the second

be improvement and the patient may get used to the condition, it is a persistent source of complaint for many. In addition, in the early weeks after operation there is often a hyperaemia of the conjunctiva, objectionable on account of its appearance, and distressing because of a "gritty" sensation in the eye (Fig 421).

2. *Nasal obstruction.*—This results from hyperaemia of the nasal mucosa. It may be severe and has in one of our patients caused vacuum headaches from obstruction of the fronto-nasal duct. The obstruction tends to lessen after some months and can be relieved by ephedrine nasal drops.

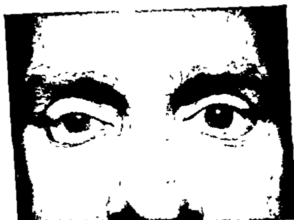


FIG 421
Horner's syndrome Note the drooping of the eyelid, the enophthalmos and the smaller pupil on the right side.

3. *Dandruff or "scurf" of the scalp.*—We have seen two patients who complained bitterly of dandruff due to anhydrosis of the scalp, and most others on questioning will admit the presence of this.

For the above reasons we believe that the advantage of the possibly slightly prolonged period of freedom from recurrent sympathetic activity following removal of the stellate is outweighed by the disadvantages which follow denervation of the head and neck. Furthermore, any sympathectomy more extensive than is necessary to denervate the affected part is undesirable as sometimes there is compensatory sweating in unsympathectomised parts of the body, *e g* around the abdomen, and this may be an unpleasant and distressing symptom.

TECHNIQUES

THE ANTERIOR OPERATION —An incision two inches long is made half-an-inch above and parallel to the clavicle starting over the inner border of the clavicular head of the sternomastoid and extending laterally (Fig. 422). The

months. This may be result of nerve impulses arising in the outlying sympathetic ganglia lying on the brachial plexus,[9,10] but why activation of these should be delayed for some months is difficult to understand. Haxton[7] considers it more probable that regeneration of the sympathetic nerve fibres is the cause of the recurrence, a view held by others.[11] The regeneration theory is supported by the following observations:—

1. Sympathetic activity in the hand is absent after pre- or post-ganglionic section.

2. Vasomotor tone returns in nearly all cases, but the latent period is longer when stellate ganglionectomy has been done as the fibres have to grow much greater distances than after pre-ganglionic section.

3. Sympathetic activity reappears gradually and increases but remains sub-normal even many years after operation, suggesting that even a few of the fibres are enough to restore full functional continuity.

4. The return of activity varies from limb to limb, even if the same operation has been done.

5. Naked eye and microscopic evidence of regrowth of sympathetic fibres has been observed after excision of the stellate and second thoracic ganglia in man.[3] Furthermore, paravertebral block by procaine in the region of the excised second or third thoracic ganglia results in temporary disappearance of sympathetic activity in a hand in which such activity has reappeared after surgical removal of these ganglia and the intervening chain.

There seems little doubt therefore that recurrence of sympathetic activity after cervical sympathectomy is due to regeneration of divided nerves, though it cannot be denied that activation of outlying ganglia possibly plays a part.

It seems that Smithwick's intraspinal root section of the second, third and fourth thoracic nerves to discourage regeneration has little advantage as the main supply to the upper limb arises from below the fourth thoracic segment. The sympathetic nerves for the upper limb grow up from the divided chain to join and follow the spinal nerves, and of necessity they must be post-ganglionic fibres which have relayed in the thoracic ganglion, for pre-ganglionic fibres cannot regenerate through post-ganglionic routes.[12] Neither does capping or clamping of the chain below stop the outgrowth of new pre-ganglionic fibres as these rapidly fill the cap and soon overflow, and this manoeuvre has not significantly lengthened the time before sympathetic activity returns.[13]

Removal of the cervico-thoracic ganglion as well as the second and third ganglia delays somewhat the return of sympathetic activity, possibly because the distance to be covered by regenerating fibres is greater, but the effects of denervating the head and neck are sometimes considerable and a source of distress to the patient. They consist of:—

1. *Horner's syndrome*.—This, consisting of enophthalmos, drooping of the upper eyelid, constriction of the pupil with sometimes blurring of vision, is a disability not lightly to be inflicted. Although after some months there may

anterior scalene muscle to separate it as far as possible from the divided chain below. The sternomastoid muscle and the cervical fascia are sutured and the wound is closed without drainage. Both sides can be operated on at the same time and the patient is allowed out of bed the following day (Figs. 423, 424).

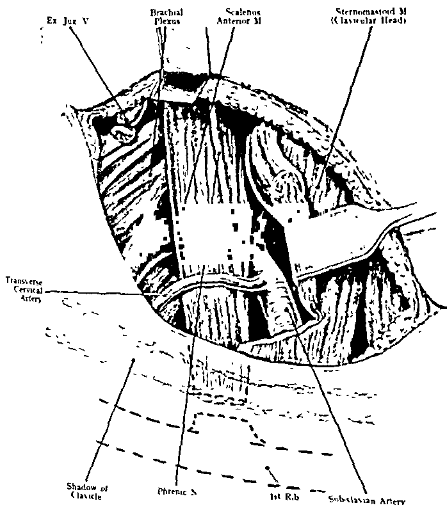


FIG 423

THE POSTERIOR OPERATION *—The patient is placed in the prone position with firm pillows beneath the upper thorax and pelvis so that there is no compression of the abdomen The arms are plac... sufficient ... being carri... This trach... should be used. ... the ... Intra-

* Reproduced by kind permission of Dr. R H Smithwick.

platysma is divided in the line of the incision and the external jugular vein identified in the outer angle is also divided. The clavicular origin of the sternomastoid is then cut. In the outer part of the wound is seen the posterior belly of the omohyoid and division of this introduces the operator to the fibro-fatty layer beneath the deep cervical fascia in which tissue is found the transverse cervical artery and vein. These vessels should be ligated and divided, except when the operation is being done for obliterative arterial disease when the artery is preserved if possible as it serves as a useful collateral. At this stage the scalenus anterior muscle is readily felt with the finger, standing out as a firm rounded vertical band the size of a little finger. The tissue overlying the muscle is swept downwards by a small swab to reveal the phrenic nerve passing on its anterior surface from above and laterally to below and medially Emerging from beneath the outer border of the scalenus anterior is the brachial plexus and the third part of the subclavian artery (Fig. 423).

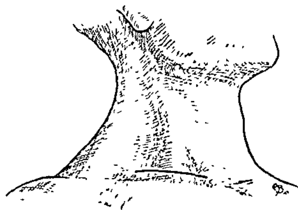


FIG. 422
Incision for the anterior operation.

The insertion of the muscle into the first rib is nibbled through with fine blunt-pointed scissors. On the right side division of the muscle is completed, but on the left side a few medial fibres are left intact to protect the thoracic duct, which is not usually seen in the course of the operation. In most patients the operation can be completed below the arch of the subclavian artery, but if access is insufficient, the arch of this vessel is depressed after division of the branches arising from its convexity. These vessels are the thyroid axis, the costocervical trunk, and more laterally unnamed and frequent anomalous ascending cervical arteries Whether approach is above or below the subclavian artery the next step is to seek with the forefinger the neck of the first rib over the apex of Sibson's fascia. This can then be dissected by the finger from the inner border of the rib, starting at its neck. The finger then elevates the pleura from the necks and adjacent shafts of the upper four ribs A malleable copper retractor is then inserted to hold down the apex of the lung A flexible light is essential at this stage and this also is inserted. The ganglionated trunk is seen running almost directly backwards, following the concavity of the upper chest wall and on its outer side and closely associated with it is the superior intercostal artery; if this vessel is damaged haemorrhage can be profuse. As each ganglion lies just below the relevant rib, the third ganglion is readily detected and the chain divided below it. The upper end is held firmly forwards to assist in division of the rami of the third and then the second ganglion. The upper end of the chain is stitched into the upper divided end of the

rib has been identified, the overlapping edge of the iliocostalis and longissimus cervicis muscle is divided to expose the articulation of the rib and transverse process. The intercostal muscles are then separated by sharp (scissors) dissection from the upper and lower borders of the rib, and the inner 4 to 5 cm. are removed, including the periosteum. If one divides the external intercostal muscle and the fascia between it and the internal muscle layer close to the rib, one can then pass a finger around the rib, outside the periosteum but between it and the pleura The intercostal nerve, artery, and vein, separated with the muscle, should not be injured. This technique is preferable to subperiosteal resections in this region. The tip of the transverse process can be removed with rongeurs, and the underlying remnant of rib is removed for 2 cm. or so.

The next step is to separate the pleura with a finger to the mid line of the vertebral column, to a point above the second and below the fourth rib, and laterally to the resected rib end The fourth rib is then resected in a similar manner. The third intercostal bundle with the exception of the nerve is then removed. The third intercostal nerve is readily visible in the middle portion of the wound, the second being concealed beneath the second rib in the upper portion of the wound, while the fourth intercostal nerve is seen crossing the lower portion of the wound. The following manoeuvre is then carried out. It is called intraspinal root section and is designed to prevent regeneration from the second, third, and fourth thoracic segments. When the third intercostal nerve is picked up with a hook, make certain that the intercostal artery and vein are not included. The nerve is divided at the lateral extent of the incision. It is followed to the intervertebral foramen, dividing the communicating rami running from the anterior aspect of the nerve to the corresponding thoracic ganglion A dental spatula can then be slipped about the dorsal branch of the intercostal nerve, and this is divided. This branch runs vertically and posteriorly between the transverse processes and is given off just lateral to the posterior root ganglion The latter then comes into view, and the spatula is inserted between the anterior and posterior roots at the proximal end of the ganglion The posterior root is divided with a knife against the spatula blade, leaving the anterior root intact. The arachnoid is then pushed medially with the spatula and separated from the anterior root, so that the latter is white and glistening and is free in the foramen. A small spinal-fluid leak results. The root is then divided with scissors, so that its lateral centimetre is removed.

After the rhizotomy has been completed, the sympathetic trunk is palpated. It lies on the anterolateral aspect of the vertebral column exactly where the head of the rib contacts the vertebral body. It is picked up on a nerve hook between the second and third ganglia. The second, third, and fourth sets of communicating rami are clipped and divided. The trunk is clipped and divided just below its fourth ganglion. The latter is cut away, and the decentralised second and third ganglia are encased in a silk cylinder.

A paravertebral incision about 7 cm. long is made and centred opposite the space between the second and third thoracic spinous processes. It is placed 4 cm. lateral to the mid-line. After careful application of skin towels. the incision is carried down through the deep fascia to the trapezius muscle. The fibres of the latter are incised vertically for several centimetres in the centre of the incision. This exposes the underlying rhomboid, which is divided

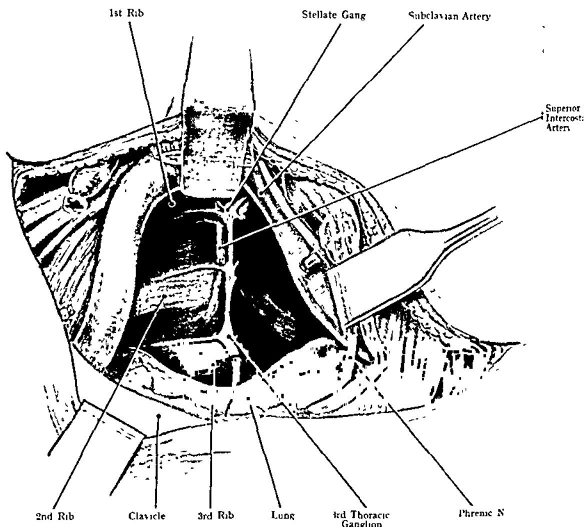


FIG. 424

obliquely in the direction of its fibres. A finger can then be passed upward and downward beneath this muscle and the ribs palpated and counted accurately. If the incision is properly placed, the oblique split in the rhomboid will lie directly over the third rib. The first rib is sometimes a little difficult to feel. The second is very prominent, and can easily be mistaken for the first If one feels carefully over this prominent rib the first will be identified with certainty. An X-ray is essential to exclude a cervical rib. When the third

rib has been identified, the overlapping edge of the iliocostalis and longissimus cervicis muscle is divided to expose the articulation of the rib and transverse process The intercostal muscles are then separated by sharp (scissors) dissection from the upper and lower borders of the rib, and the inner 4 to 5 cm. are removed, including the periosteum. If one divides the external intercostal muscle and the fascia between it and the internal muscle layer close to the rib, one can then pass a finger around the rib, outside the periosteum but between it and the pleura. The intercostal nerve, artery, and vein, separated with the muscle, should not be injured. This technique is preferable to subperiosteal resections in this region. The tip of the transverse process can be removed with rongeurs, and the underlying remnant of rib is removed for 2 cm. or so.

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The distal stump is then sutured to the intercostal muscle in the upper portion of the incision.

THE AXILLARY APPROACH.[5,15]—An approach to the upper thoracic paravertebral chain can be made via the second intercostal space in the axilla. The patient is placed in the lateral position with the side to be operated on uppermost, and the arm extended. An incision 7 cm. long is made over the second intercostal space, extending backwards from the margin of the pectoralis major. Care is taken to avoid the long thoracic nerve of Bell which may be seen in the posterior angle of the incision. The pleural cavity is opened in the line of the incision, and a rib retractor inserted. The apex of the lung is depressed by long illuminated retractors and over the necks of the ribs can be seen the paravertebral chain beneath the parietal pleura. Removal of the second ganglion alone was originally suggested, but this leaves a very small gap to be bridged by regenerating fibres, and it is wiser to remove the second, third and fourth ganglia. Care must be exercised to avoid injury to the superior intercostal artery, as control of this vessel in such a deep cavity is difficult. Apical pleural adhesions may complicate the operation, but the parietal pleura can be dissected downwards and the operation performed extrapleurally to avoid this hazard; but extrapleural haematoma may follow.

The advantage of the operation is the ease with which it is performed, and the avoidance of a dissection at the root of the neck. Its disadvantages are that an intercostal incision with rib retraction is often followed by pain, and there is difficulty in controlling occasional accidental haemorrhage from the superior intercostal artery. Any manoeuvre designed to prohibit or delay regeneration of sympathetic fibres is difficult It is sometimes a useful operation in obliterative arterial disease involving the subclavian or axillary arteries, as all important collateral vessels are avoided.

A modification of the Telford operation has been suggested which on theoretical grounds is certainly worthy of trial.[3] After division of the rami of the second, third and if possible the fourth ganglia the chain is divided just below the first. Through a stab incision in the back, a pair of forceps is introduced into the chest through the third space, the points of which grasp the lower end of the divided chain and withdraw it, to stitch it to the dorsal muscles This could be expected to delay new sympathetic fibres from below making contact with the brachial plexus (Fig 420E).

There is little difference between the rate and degree of return of sympathetic activity whether the Telford or the Smithwick operation is done The latter is followed by more post-operative discomfort, the scar is more prominent, and both sides cannot be done at the same session; for these reasons the anterior route seems the more advisable.

LUMBAR SYMPATHECTOMY

Removal of the second and third lumbar ganglia with the intervening chain results in sympathetic denervation of the leg below the knee. In order to sympathectomize the thigh, the first lumbar ganglion must be removed also. In practice it appears to make little difference whether the first ganglion with the second and third, or whether only the second and third are removed. Excision of the first ganglion on each side usually results in loss of power of ejaculation in the male and unless it is really essential from the point of the circulation, they should not both be removed. Although some consider excision of the first lumbar ganglion advisable[16,17] others are not so impressed by the importance of the first and the usual operation is removal of the second and third only. Using a precise technique for the detection of sudomotor activity, Hertzman[18] thinks that complete sympathectomy of the lower limb is reasonably certain only after removal of the whole lumbar chain, and possibly the twelfth thoracic ganglion as well. It is not always complete even after this extensive operation. Ross[19] considers that the second and third ganglia should be excised when the arterial obstruction is at or below the level of the femoro-popliteal junction, but that the first should also be excised when the obstruction is in the upper part of the femoral artery, or above this level. This seems to us to be the reasonable approach to the problem, and has been our practice

The fourth ganglion should not be excised as its removal contributes nothing to the completeness of the operation[17]

Transperitoneal approach.—This is the operation of choice when there is obstruction of the iliac vessels or the aorta. To avoid damage to important collateral vessels in the abdominal wall a mid-line incision[20] centred on the umbilicus is used On the left side the peritoneum is divided lateral to the descending colon and *the splenic* flexure The whole of the descending colon with its leaf of mesentery is dissected off the posterior abdominal wall by blunt dissection and held *over to the right* by a large sponge and the arteries of supply to the colon, the testicular or ovarian arteries, and the left ureter are carried over with the peritoneum. The angle between the medial border of the psoas and the aorta is *exposed and in* this angle can readily be felt the sympathetic cord and its ganglia. The fourth ganglion is constant in position at the level of the bifurcation *of the* aorta, and rather tucked beneath the common iliac artery This ganglion is cleared by blunt dissection, and the chain divided immediately above. *The* upper end of the [illegible]
seized by [illegible]
second an[illegible]
this level [illegible]
[illegible] ganglia and the cord between the first and the fourth is very variable, and there may be one ganglion, often considerably elongated, representing the second *and* third *The chain* between ganglia may also be double or triple but the multiple strands always reunite at ganglia[21]

Rarely on the left side, but frequently on the right side lumbar veins pass in front of the chain, and traction on these renders them similar in appearance to a communicating ramus. If they are divided in error, they must be sealed by diathermy or ligated. The lumbar arteries do not pass in front of the cord and should not be damaged during the operation.

Removal of the first lumbar ganglia is difficult by the transperitoneal route, and necessitates firm retraction upwards exposing the medial lumbo-costal arch, beneath which the sympathetic chain disappears. The arch is bloodless and is divided for about 2 cm. when the first lumbar ganglion can be seen and removed.

Sometimes it may be difficult to ensure that all the sympathetic fibres, when multiple, have been removed, and clearing of all the tissue over the anterolateral aspect of the lumbar vertebrae can be done to ensure complete removal, but if the ganglia are clearly defined and removed, all significant sympathetic nerves will be removed also.

On the right side a similar procedure is carried out after mobilisation of the caecum, ascending colon and the hepatic flexure, the ureter being guarded. Careful retraction of the inferior vena cava must be exercised to avoid damage to it or its tributaries.

LUMBAR APPROACH.—The lumbar approach is less disturbing to the patient, and the operation is carried out without entering the peritoneal cavity. Both sides can be operated on at the same session with little more disturbance to the patient than unilateral operation It is the standard method of approach and should be used except when the arteries of the abdominal wall are functioning as important collateral channels.

The patient lies flat on the operating table, and guards are rigged on each side so that when the patient is tilted laterally he cannot roll off The abdomen is prepared and towelled from the axillary line on one side to a corresponding line on the other side if the operation is to be done bilaterally, and from the ziphisternum above to midway between the umbilicus and the pubis below. If only one side is to be operated on, only half the abdomen is so prepared The table is then tilted laterally to 35°, and the uppermost side is operated on first. An incision six inches long is made starting over the tip of the twelfth rib and extending downwards and inwards in the line of the fibres of the external oblique. The external oblique is split to expose the internal oblique, which muscle and the transversalis muscle beneath are also split in the line of their fibres. The peritoneum is not opened but is gently dissected off the underlying muscles of the lateral and posterior abdominal walls until the medial border of the psoas major muscle is reached. The ureter adheres to the peritoneum, and must be identified. Lying on the psoas muscle can be seen the genito-femoral nerve. The operation then proceeds in the manner described above. The first ganglion can be reached after firm retraction upwards by a Deaver or similar retractor, if its removal is considered necessary The muscles are sutured and the skin incision is closed. The operating table

is then tilted to 35° in the opposite direction, and a similar procedure is carried out (Figs 425, 426, 427, 428).

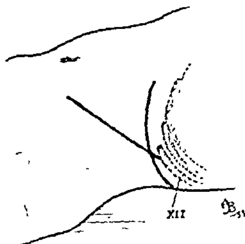


FIG. 425
Alternate incisions for the operation of lumbar sympathectomy Sometimes removal of the twelvth rib is undertaken, but in this case, operation can hardly be done on both sides at the same session.

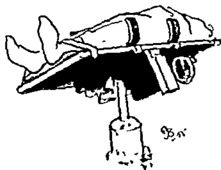


FIG 426
With the patient properly secured, the operating table is tilted and the uppermost side is operated on first. Tilting in the opposite direction is followed by the contralateral operation.

If a tilting operating table is not available, sandbags should be placed under the shoulder, chest and pelvis to cause sufficient tilting of the patient for the abdominal contents to fall away from the side to be operated on

but after one side has been done the patient will have to be disturbed and redraped for transference of the sandbags to the other side.

When both sides are to be operated on at the same session we think it is better not to move the patient more than is necessary, and for this reason

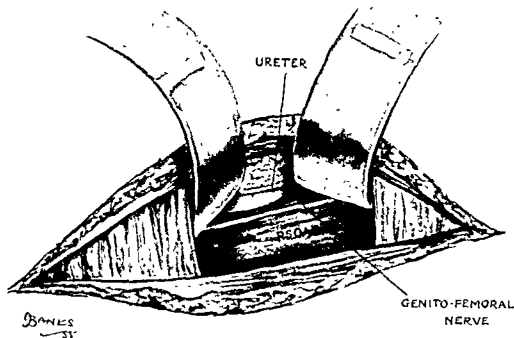


Fig. 427
The exposure is via a gridiron incision.

do not employ the slightly more easy lateral approach via a transverse incision in the flank, immediately below the twelfth rib. In this approach there is considerable disturbance in moving the patient from one side to the other If only one side is to be operated on, then the lateral approach is simplest

It is important that the operation be done expeditiously, and with minimal blood loss to avoid post-operative shock or hypotension as this might well lead to thrombosis in an artery already diseased. The bilateral operation can readily be completed in half-an-hour.

The patient is allowed out of bed the day after operation, and activity is encouraged in order to lessen the chance of venous thrombosis, and chest infections. The operation, even done bilaterally, is accompanied by remarkably few complications, although a rather high incidence of post-operative venous thrombosis has been reported.[22] In our series of 157 patients on whom the bilateral operation had been done there were four deaths, an operative mortality of 2·5 per cent.

After lumbar sympathectomy a rather common complication is a neuralgia-like pain in the thigh, often associated with inability to rest and relax the limb. The cause of this is not clear, but it occurs in about 12 per cent. of patients It always—sometimes rather suddenly—disappears after three weeks to three months, and the patient can be safely reassured.

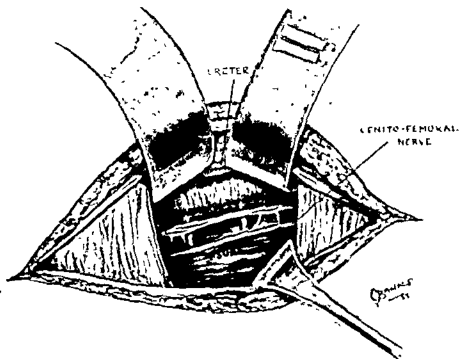


FIG 428
Sometimes retraction of the psoas muscle is necessary before exposure of the sympathetic chain is made

PARAVERTEBRAL INJECTION OF THE THORACIC SYMPATHETIC TRUNK [21]

The highest prominent spine of the vertebral column is the seventh cervical, and this marks the level of the first rib. The tip of the spine of any thoracic vertebra is opposite the rib from the vertebra below. A wheal is raised 1½ inches lateral to the spine of the vertebra above the ganglion to be injected and through this is inserted a four-inch needle perpendicularly until contact is made with the transverse process at a depth of 1 - 1½ inches. The point of the needle is eased below the transverse process, inclined inwards about 20° and advanced another 1 - 1½ inches, when contact should be made with bone again A rubber marker on the needle will assist in judging the depth of its point The sympathetic chain lies about 1¼ inches beyond the transverse

process, and the angle of the needle must be changed if the side of the body of the vertebra is felt at less than this distance, or if no bone is felt at more than this distance. The point of the needle should be as far forward as is possible, provided it is in contact with the vertebral body when the injection is made, and the further forward it is the less likelihood is there of injecting in the region of the somatic nerve. Aspiration is done before the injection to avoid injection into a vessel or into the subarachnoid space. Procaine 2 per cent. in a dose of 2·5 ml. will cause temporary paralysis of the sympathetic ganglia, and if this amount rapidly produces anhydrosis of the hand the needle is correctly placed.

If prolonged paralysis of the sympathetic chain is required, as in angina pectoris, 4 - 5 ml. of 95 per cent. alcohol is injected after the position of the point of the needle has been verified by the effect of injection of 2 - 3 ml. of 2 per cent. procaine.

Puncture of the lung has led to tension pneumothorax, and after alcohol injection intercostal neuritis may be troublesome, but it usually clears up in a month or two.

PARAVERTEBRAL INJECTION OF THE LUMBAR SYMPATHETIC TRUNK[23]

The patient lies on the side opposite to that to be injected. A needle, four inches long, is inserted through a local wheal of the skin two inches lateral to the upper margin of a spine of a lumbar vertebra. The point of the needle is advanced perpendicularly to a depth of about 1½ inches, when the transverse process of the same vertebra is felt. The point of the needle is then edged over the upper margin of the transverse process, and inclined inwards to impinge on the side of the body of the lumbar vertebra at a depth of about 1 - 1½ inches beyond the transverse process. A rubber marker on the needle is a help to insure the correct depth of the needle point. The syringe should not be attached to the needle until the point is in place in order to avoid injection into a blood vessel or even the subarachnoid space and, before the injection is made, a test aspiration is done. If after injection of 2·5 ml 2 per cent. procaine the foot on that side becomes warm and dry, the point of the needle is correctly placed, and if prolonged paralysis is required an injection of 4 - 5 ml. of 95 per cent. alcohol or 10 per cent. phenol[24] can be made relatively safely, although in the latter case paraplegia has occurred more than once, and neuritis is common

The second and third lumbar ganglia can be injected to sympathectomize the lower limb, the needle being inserted at the levels of the upper borders of the spines of the second and third vertebrae.

AMPUTATIONS

Tourniquets are best avoided in operations performed for obliterative arterial disease.

TOES.—In patients with ischaemia, healing of the stump after amputation of or through a toe may be precarious. In order to damage as little as possible the existing patent vessels, a circular incision around the phalanx is made dividing all tissues down to the bone. Flaps should not be made The bone is cut through with bone forceps The proximal part of the divided phalanx is then nibbled out with fine bone nibbling forceps as far as the interphalangeal or metacarpo-phalangeal joint, and the cartilaginous head of the proximal phalanx or of the metacarpal is similarly nibbled away. No vessels are tied, and the wound is not stitched, or at most one stitch is used to approximate loosely the wound. A loose dressing of tulle gras, or gauze soaked in Bradosol (1 : 2,000) is applied and left undisturbed for seven days Healing is usually complete in seventeen to twenty-one days, a small terminal scar remaining.



FIG 429
A five-inch stump of tibia should be left

BELOW KNEE AMPUTATION.—With the patient lying on his face, unless the prone ... patient, and ... is measured ... ...ior flaps are ... the deep fascia is divided at the same level, and the flaps including the deep fascia are reflected upwards with the utmost gentleness to the line of section of the tibia The muscles are cut transversely at the level of bone section and after all vessels have been secured the tibia is divided. It is wise to bevel the subcutaneous crest of the tibia before the transverse saw cut is made The fibula is divided about one inch above the level of the tibia (Fig. 429) The deep fascia is sutured over the bone ends with interrupted catgut stitches and the periosteum can be used over the subcutaneous border of the tibia where there is no deep fascia. The skin is sutured with vertical mattress stitches, after careful approximation of the edges A corrugated rubber drain is carried across the wound to emerge at the medial and lateral corners It is not anchored to the skin Dressings and a sterile bandage are firmly applied over cotton wool, leaving one end of the corrugated drain outside the dressing This end is then covered with a further sterile dressing, and the whole is bandaged again The drain is removed after forty-eight hours without disturb-

ance of the first bandage. The dressing is removed after ten days, and the stitches taken out. Movements of the knee joint are encouraged, and in order to avoid pressure on possibly devitalised tissue we do not use a splint that some have advised. Flexion contracture has not occurred in our experience.

AMPUTATION BY CIRCULAR INCISION.—Silbert[25] has suggested, and others have recommended,[26] a circular incision through the skin five inches distal to the tuberosity of the tibia. No forceps are applied to the skin, which is handled



FIG. 430
Through-knee amputation The horizontal part of the incision passes just above the tibial tubercle

with extreme gentleness. The skin flap is retracted, the muscles are incised transversely down to the bone, and the bones are divided higher up. The flaps are brought down, and kept in place by a vaseline gauze bandage. No stitches are inserted. The dressing is untouched for a week, and at the end of this time, if the skin appears healthy, approximating sutures are inserted, or if there is any doubt about the condition of the skin these are omitted. Healing occurs after three to four weeks, leaving a terminal scar.

This operation was first described for patients with diabetic gangrene, and it was successful in seventy-five out of seventy-eight consecutive operations, three requiring re-amputation on account of the use of a tourniquet. It has been suggested that the same operation be used for atherosclerotic gangrene, whether associated with diabetes or not.

"THROUGH KNEE" OR STOKES-GRITTI AMPUTATION.—The flaps consist of a long anterior one including the patella and short posterior segment. The anterior incision starts at the adductor tubercle of the femur, sweeps downwards and crosses the tibia just above the level of the tibial tubercle, and ascends to a point over the outer condyle of the femur corresponding to the adductor tubercle on the inner side The posterior flap is made by joining the points of origin of the anterior flap by an incision slightly convex downwards. The patellar tendon is divided at the lower border of the patella, the knee joint is opened and the structures behind the joint are divided at the same level The femur is then sawn through just above the adductor tubercle, and the joint surface of the patella is sawn off The patella is drawn down

and placed over the lower end of the divided femur, and kept in place by a silk suture, which may have to be inserted through the bone as the remnant of the patella ligament does not readily retain sutures (Figs. 430, 431). A corrugated drain is inserted as described previously, and the skin edges, lying well posteriorly, are sutured. The stump heals well without complication and in the elderly a useful end-bearing artificial limb can be fitted in six to eight weeks' time. This is the great advantage of this operation; elderly patients can soon be ambulant (Fig. 432).

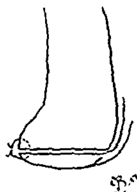


FIG. 431

ABOVE KNEE AMPUTATION.—A ten- to twelve-inch femoral stump is ideal, with an anterior flap longer than the posterior. The skin is marked at the level of bone section. The total lengths of the anterior and posterior flaps should just exceed the diameter of the limb at the site of section, and the anterior should be twice as long as the posterior flap. So that the flaps' edges may be sutured without discrepancy the base of the anterior must be considerably less than the base of the posterior flap. The deep fascia is divided with the skin and is reflected up to the level of bone section, and the muscles are divided transversely at *this level*. The artery in the substance of the sciatic nerve must be tied with the other patent vessels of the limb and when haemostasis is secure the deep fascia, rather defective posteriorly, is sutured over the end of the stump. The skin flaps are sutured by vertical mattress sutures, and a corrugated drain is left *in situ* as described previously. The stitches are removed on the tenth day, and before this time exercises to maintain extension and adduction are started. After three weeks the stump is bandaged to achieve a proper conical shape, if there is reasonable expectation that the patient will use an artificial limb (Fig. 433).

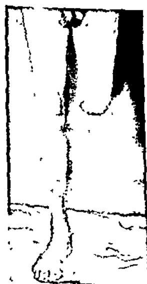


FIG. 432
Amputation through the knee-joint

Occasionally, *especially* in thromboangiitis obliterans which involves the vessels higher and higher in the limb in successive waves of activity, and sometimes in aortic obstruction from atherosclerosis with a recent superadded thrombosis, an ever higher amputation may be necessary.

AMPUTATION OF FINGERS.—This operation is never required in atherosclerosis, rarely in thromboangiitis obliterans. On the few occasions when we have had to amputate a finger, a dorsal racket incision has been used, and healing has been uneventful.

AMPUTATION OF TOES WITH THEIR METACARPALS IN INFECTIVE GANGRENE IN ASSOCIATION WITH DIABETES.—In patients with gross sepsis arising in the toes and involving the foot, when suppuration spreads up and around the shafts of the metatarsals, adequate drainage must be secured. The affected digits, their metatarso-phalangeal joints, and the shafts of the metatarsal bones

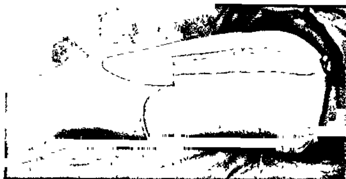


FIG. 433
A ten-inch femoral stump is the ideal, but it can be less if it is considered that the patient will not manage an artificial limb

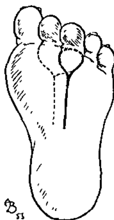


FIG. 434
Through the plantar incision one or more metatarsals and their digits can be excised

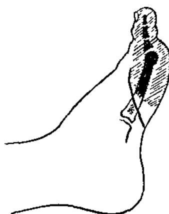


FIG. 435
The plantar incision must be long enough to ensure free drainage of the infected tissues with the patient lying in bed

up to a level where their periosteum is no longer separated by pus, must be removed through an incision in the sole of the foot, branching to encircle the digit or digits to be removed (Fig. 434). The vertical limb of the incision must extend sufficiently far for drainage to be effective, without pocketing of pus, with the patient lying in bed (Fig. 435). The wound can be powdered with streptomycin and parenteral antibiotics are given Gas-forming organisms are almost always present, but though prior to operation toxaemia may be

severe, the rapid pulse of gas gangrene toxaemia is not seen and involvement of muscle tissue does not occur. When proper drainage has been secured, healing is remarkably rapid, and the foot, though grossly deformed, is painless because of the co-existing neuritis

METHODS OF TEMPORARY CONTROL OF ARTERIAL FLOW

An artery may be temporarily controlled by a tape of rubber tube or soft broad Paul's tube around it, tightened sufficiently to obstruct the blood flow. The chosen material can be held tight with artery forceps. Less damage to the artery is suffered if a piece of rubber tubing, the size of the vessel to be ligated, is incorporated in the ligature Bulldog clamps and Pott's patent ductus clamps are also used, but Blalock's clamp, unless the blades are covered with cotton socks, may seriously injure the vessel. We prefer Pott's clamp for larger vessels, and bulldog clamps for smaller tributary vessels (Figs 436 and 437).

Such temporary control of a large artery the seat of marked calcification may be difficult, but we have in fact never witnessed, though we have feared, fracture of a calcified plaque, nor have we seen any complication resulting from injury of an artery which has been so managed.

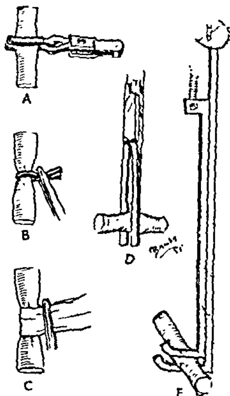


FIG 436
Methods of temporary ligation of artery.
A Bulldog clamp B. Rubber tube C. Paul's tube D. Pott's clamp. E. Blalock's clamp


FIG 437
Rubber tube incorporated in ligature The tube should be about the same size as the artery to be ligated

ARTERIAL REPAIR

Certain wounds of arteries can be repaired successfully A longitudinal or slightly oblique clean incised wound of an important artery is suitable for repair by suture A transverse incised wound, if less than one-third of the circumference of the artery, can be sutured, but if more of the circumference is divided it is better to complete the division, and do a formal end-to-end suture Only if the wound in the artery is cleanly incised and free from bruising on either side should repair be done. If the injury results from penetration of a blunt or ragged fragment, or from within by a bone fragment, there is some concussive effect with intimal damage spreading beyond the

site of apparent injury. In this case excision of the damaged segment, including 1 cm. of apparently normal vessel, must be done and repair effected, in most cases by a graft. Opportunities for repair of incised wounds of arteries must be rare; knife wounds are not common and in this country are most often seen in butchers (Fig. 438).

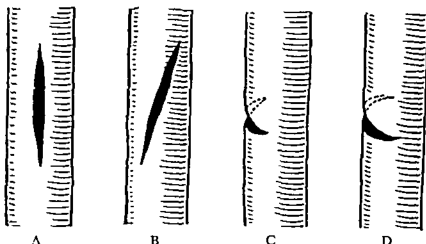


FIG. 438

A, B, and C might be suitable for repair if they have been caused by an incised wound

D This wound should be resected, and end-to-end suture done, or if necessary a graft inserted

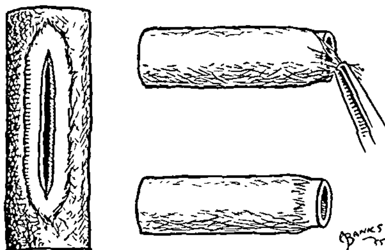


FIG 439

The adventitia is dissected off the vessels before suture

Before arterial suture the adventitial layer must be dissected away from the incision in the wall of the vessel (Fig. 439) From the end of the vessel it can be drawn down and cut across so that when it retracts the vessel remains projecting from its coat. Suitable material for suture is 00000 silk or the synthetic material Samolene, of the same size which is stronger and which

raws through the arterial wall more easily. The thread should be mounted n an eyeless needle and lubricated with sterile liquid paraffin before use.

When repairing a linear tear in an artery, stay sutures are first placed at ither end, and held under slight tension. This steadies the segment to be epaired, and a through and through stitch is inserted at 2 mm. intervals, with careful approximation of the intima (Fig. 440).

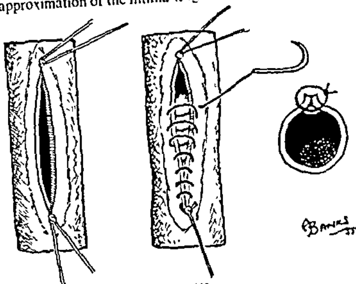


Fig. 440

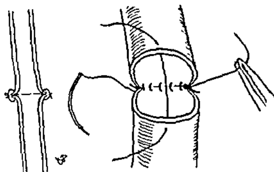


Fig. 441

End-to-end suture of a divided artery is done by triangulating the vessels with three stay sutures inserted equidistantly around the circumference. The segments between the stay sutures are stitched in turn (Fig. 441). A continuous suture is quite satisfactory, but if the sutured vessel is that of a growing child, then interrupted sutures should be used, at any rate over half the circumference. Everting mattress sutures tend to constrict the anastomosis line Sometimes it may be difficult to approximate the ends of a divided vessel. Additional length may be obtained by mobilising the vessel, but this must be done with extreme care to avoid injury to an important collateral branch. If approxima-

tion is impossible, after the loss of a segment of an artery, it is better to insert an autogenous vein graft. When the controlling tourniquet is released bleeding generally occurs from the suture line, but gentle pressure of a sponge for a few minutes usually stops the bleeding. If this fails some "borrowed" adventitial layer from a nearby segment of artery will often control the leak, but occasionally it may be necessary to put in an extra stitch, though this should be avoided if possible for each added stitch narrows the lumen a little more.

EMBOLECTOMY

Before heparin was available, successes after embolectomy were unusual After its introduction the operation was more successful, but heparin also became the mainstay of conservative treatment and there is considerable doubt whether operation has much, if anything, to offer which cannot be achieved by the non-operative management, at least in vessels distal to the bifurcation of the femoral artery. Operation should be advised in embolism of the bifurcation of the aorta, and of the common iliac arteries. The indications for embolectomy distal to this site, and in the upper limb, are discussed in Chapter XII.

Successful restoration of the circulation after embolectomy depends on the following prerequisites:

1. Early operation—the earlier embolectomy is done the more likely it is to be effective. Successes are rare more than ten hours after embolism
2. Wide exposure of the vessels above and below the site of embolism.
3. Careful dissection of the vessel or vessels distal to the site of lodgement, with control of flow by tape or rubber. These vessels are occluded not only for haemostasis but also to prevent the passage of clot which may be broken from the embolus during manipulations for its removal.
4. Control of the main vessel proximal to the bifurcation.
5. Clearance of the adventitia from the vessel over the site of the proposed incision.
6. Incision of the main vessel over the embolus, extended upwards above the embolus, but not so far distally to encroach on a bifurcation, so that, when the incision is sutured, the origins of the branches are not narrowed
7. Extraction of the clot by means of a rubber suction tube with utmost care not to scratch or damage the intima. To complete removal of any clot, the distal tourniquets are temporarily released, one at a time, with the hope that retrograde flow will wash out any fragments of clot. The proximal tourniquet is then similarly released, and for the same purpose, and then the lower tourniquets are released again. If retrograde flow is brisk, and the clot not adherent at any point, then there is a good chance of the operation being successful. After the clot has been removed, the lumen of the vessel and the field of the operation are gently syringed with sodium citrate or heparin solution and irrigation is continued until the vessel has been sutured

8 Careful suturing of the artery with lubricated sutures on an eyeless needle.

THE USE OF ANTICOAGULANTS.—In peripheral embolectomies anticoagulants are used. The operation wound is frequently examined for early evidence of bleeding. A haematoma if it occurs may perhaps be aspirated, but it is probably wiser to open a wound in which bleeding has occurred.

After embolectomy from the aortic bifurcation, or from the common iliac artery, if done through an incision directly into the vessel, anticoagulant therapy is dangerous Any haemorrhage may be obscured until loss of blood is considerable

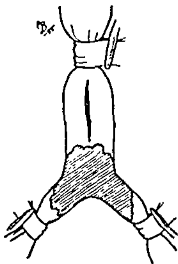


FIG 442

AORTIC EMBOLECTOMY.—*Indirect operation*—Emboli can be removed from the aortic bifurcation through incisions into the femoral arteries exposed in both groins. Each femoral artery is temporarily occluded, and then opened above this level by a longitudinal incision If the history of the patient reveals which femoral artery was first to be obstructed, this one is opened first, as the larger part of the embolus is on this side The embolus may be freed sometimes by suction, sometimes by abdominal massage if the patient is thin, or if these methods fail, then the abdomen must be opened through a gridiron incision, and the embolus milked along the iliac vessels until it can be removed from the opened femoral vessel. The same procedure is then carried out on the other side.

Direct operation—Direct approach to the aortic bifurcation can be made via a left paramedian incision, one-third above and two-thirds below the level of the umbilicus, and after control of the iliac arteries, and then of the aorta above the bifurcation, the aorta is incised, and the clot extracted by forceps and suction (Fig. 442).

We prefer the direct to the indirect operation for the following reasons: Intravascular manipulations with a rubber sucker, or extravascular manoeuvres often necessary with the indirect approach, may damage the intima, especially if the vessel is the site of atherosclerosis; the extraction of the clot is more certain, often quicker and no more disturbing to the patient when the approach is direct

ILIAC EMBOLECTOMY—Principles similar to those applying in aortic embolectomy apply in embolism at the iliac bifurcation. The direct approach is preferred for the same reasons as those advanced for aortic embolectomy.

FEMORAL EMBOLECTOMY.—The artery is approached by an incision in the groin, preferably under a general anaesthetic, although the operation can be done under local anaesthetic if the general condition of the patient demands this.

Embolectomy from other sites is rarely indicated.

Before any embolectomy is done, an X-ray is taken to determine the presence or absence of calcification, for if this is extensive it may render repair of the artery after removal of the clot impossible. Gross calcification over the site of lodgement of the embolus is a strong indication for conservative treatment.

ARTERIAL GRAFTING

In 1912 Lexer,[27] applying the teaching of Carrel,[28] recorded three patients on whom he had replaced an arterial defect by a vein graft. Occasional successful operations were reported after this date, and in 1939 Murray[29] used autogenous vein to replace the defect caused by excision of a popliteal aneurysm, and for the first time used heparin successfully in the period immediately after operation

Since the second World War there has been an intense interest in artery grafting, and a number of important papers have appeared, although there is as yet no agreement as to the indications for grafting, nor as to the best material for grafts.

Generally, it may be said that grafting of segments of the larger vessels, such as the aorta and iliacs, is usually successful, but that grafting of peripheral *arteries, the site of atherosclerosis or thromboangiitis obliterans, is less likely* to be attended with success. Healthy peripheral arteries can be grafted after excision of a segment injured by trauma, *but when excision has been necessi*tated by obstruction from disease, success can only be expected when disease in the vessel to be grafted is minimal and localised.

Varieties of grafts

AUTOGENOUS VEIN.—Most consider that autogenous vein is the best material for replacing peripheral arteries. *The internal saphenous or the* external jugular vein can be used, vessels which are readily available , in fact the former may be obtained via the incision used to expose *the femoral artery,* which is often the one damaged. Autogenous vein will live in the tissues This was demonstrated very clearly to us in the case of a patient with obstruction from atherosclerosis of the femoro-popliteal junction on whom we did an excision of the obstructed segment and replacement of this with a venous autograft The graft was successful at first, but on the tenth day after operation there was a leak from the lower anastomosis. The site was explored, and a further suture inserted During manipulation of the graft with forceps, the transplanted vein was observed to contract firmly for several seconds, and this recurred on a second manipulation. The muscle of the vein wall was clearly

living. The use of autogenous vein, if indeed a vessel of suitable size is available, is not recommended within the abdominal cavity. Experimentally the use of vein has not proved satisfactory in this situation, the grafted segments often dilating and showing mural thrombosis.[30]

ARTERY.—Heterografts are known to be unsuccessful[31] and it is possible that a graft obtained from a donor of one race may not be suitable for a recipient of another race.[32] Homografts have been used extensively with success, but their collection and storage raises many problems. In the battlefield grafts can be readily obtained from suitable donors, and this was one of the facts which contributed to the remarkable results of the U.S. Army Medical Corps in the Korean war in the treatment of arterial injuries. Many reports of the successful use of arterial homografts have been made, and for replacing segments of intra-abdominal vessels they are undoubtedly preferable to vein. Apart from the strength of artery, it is easier to suture and it possesses a normal elasticity and pulsatility; lack of pulsatility may lead to dilatation and tortuosity not only of the main vessel but also of the collaterals.[33]

On the other hand degeneration, calcification and dilatation of grafted artery has occurred.[34, 35]

CLOTH.—The use of synthetic cloth for grafts has recently been the subject of extensive experiment. Nylon, orlon, dacron and Vinyon "N" have been used successfully in experiments and functioning grafts have been reported in man.[36, 37] A "knit" is probably better than a "weave" as it is more elastic and will pulsate to some extent. Following placement and on releasing the blood flow, haemorrhage through the graft may be alarming, two or more pints of blood being lost through the interstices of the cloth, but this ceases after a few minutes, and function appears satisfactory. The preparation of cloth grafts not so liable to leakage is being actively investigated in various centres, and promising materials have been produced.[38] Polyvinyl alcohol sponge has most of the properties required for such purposes, and clinical trials appear satisfactory. It can be readily moulded and grafts can be stored ready for use. A long follow-up will be necessary before any material can be assumed to be safe from eventual complication.

The fate of grafts.—Autogenous vein grafts probably live in the majority of instances. All other grafts die. Any homologous graft acts as a channel for the flow of blood until the host can replace the tissues of the graft, using its elastic tissue as a scaffold. A new endothelial layer grows in from the parent artery, and, most important, a new intimal lining resembling normal intima is derived from cells of the blood stream. It seems that a segment of dead artery, or cloth, is as effective as a living graft as regards function.[39, 40] The length of the graft does not appear to influence its behaviour.[41]

Methods of storage of homologous grafts.—Segments of artery removed without aseptic precautions can be sterilised by high voltage cathode-ray irradiation, and stored indefinitely in carbondioxide ice at −60° C.[42] Grafts similarly removed can also be sterilized and stored in 4 per cent. formalin buffered to *p*H 5·6, and in this there appears to be little tendency to calcification, a complication which may occur with storage in stronger formalin and alcohol solutions.

An artery removed aseptically can be kept at 4°C. in Ringer's solution with the addition of 10 per cent. homologous serum, penicillin and streptomycin, provided it is used within 4 - 6 weeks.

Freezing is the most economical method of storage. For this purpose grafts should be taken from suitable donors with healthy arteries within six hours of death, and with aseptic precautions. They are put into a chamber at a temperature of −20°C. where they can be preserved for long periods More recently Hufnagel[43] has devised and Rob and Eastcott[44] and others[45] have used and perfected a method of freeze drying after which arteries can be stored indefinitely at room temperature. The grafts are kept in sealed glass containers, the size of a large test-tube and they can be transported readily. Before they are wanted, they are immersed in saline solution for thirty minutes to rehydrate, after which tributaries are tied.

Experimental work has shown freeze dried grafts to be as effective as fresh material,[46] and this has been borne out clinically.

Aortic and iliac grafting.—A number of successful replacements of the aorta with or without the bifurcation have now been recorded[35, 37 45, 47] Fresh or preserved artery or cloth grafts should be used. Synthetic grafts will no doubt replace artery in the near future.

INDICATIONS FOR AORTIC OR ILIAC GRAFTING.—1. Saccular aneurysm of these vessels not extending so high as to involve the origin of the renal arteries should be excised and replaced by a graft Fusiform aneurysms associated with atherosclerosis rarely advance rapidly and may persist without symptoms for many years. Leaking aneurysms should be operated on as a matter of some urgency.

2. In some patients with obstruction of the aorta or iliac vessels from atherosclerosis, or after aortic embolism in those occasional patients who do not suffer immediate gangrene, the decision as to whether operation should be performed should take account of the knowledge that many live for some years with symptoms of intermittent claudication only, and without the development of gangrene. On the other hand Leriche maintains that all eventually develop gangrene. In younger persons the obstruction tends to be complete and localised; in the elderly it is more often incomplete and accompanied by diffuse disease in the iliac vessels, and

indeed throughout the limb. Operation is more usually indicated in the younger group

Peripheral artery grafting.

1. TRAUMA.—The insertion of a graft to replace a segment of artery damaged by injury is now an established and successful operation. During the recent war in Korea, a very high proportion of successes was obtained[48, 49, 50, 51] (Fig. 443). In the less frequent arterial injuries occurring in civil life, occasional successes have been recorded[12] and we have recently excised two inches of damaged femoral artery and successfully re-established continuity with a *graft of artery preserved* in buffered formalin solution. Major arterio-venous fistulae should be repaired by grafting, if necessary, as soon as possible (*see* Chap. XV).



FIG 443
Vein graft inserted to bridge a gap in the popliteal artery severed by trauma.

2. ATHEROSCLEROSIS. — Obstructed segments of artery in atherosclerosis, a

first appears when there is narrowing or obstruction, particularly of the lower part of the femoral or popliteal artery, sometimes of the upper part of the femoral or iliac artery, without arteriographic evidence of disease elsewhere in the limb In this type of case an excision of the diseased segment and replacement by graft can be considered, but a lumbar sympathectomy often does well if the obstruction is in the iliac or femoral artery and may relieve the only symptom, claudication, though it is less successful if the lower half of the femoral artery is obstructed When the disease is more extensive with irregularity of the *lumen of the larger vessels throughout the limb, grafting sometimes is successful, and it* may be tried in a patient with incipient gangrene when there is segmental thrombosis of a major vessel Some limbs have been saved from gangrene by this The results of peripheral vessel grafting in atherosclerosis have not been satisfactory in our experience, and in only one patient has the graft remained patent for more than two years Eight out of our fourteen autogenous vein grafts of femoral or popliteal arteries were immediately successful, but only five were discharged from hospital with palpable distal vessels, three being *patent at the end of a year* and one after two years Thrombosis at or about the site of a graft, shortly after operation may be cleared by insertion of a polythene tube above the level of the upper anastc

mosis and by aspiration through this of the recent thrombus, followed by heparin administration.[41] Most authorities have had an experience similar to ours,[41,54] though a few have recorded more successful series.[44,53,54] It seems

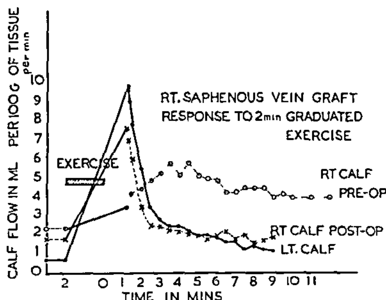


FIG. 444
The graph shows a return to normal blood flow after excision of a thrombosed segment of femoral artery and replacement by autogenous vein graft (*Postgrad med J.*)



FIG. 445
Popliteal aneurysm before excision and after the insertion of an homologous artery graft.
(*Brit J Surg*)

clear that the operation, if it is performed, should be done only after the most careful consideration (Fig. 444)

3. PERIPHERAL ANEURYSMS.—Peripheral aneurysms of syphilitic origin are often the result of a localised lesion of the artery and are therefore less liable to thrombosis than is a vessel with atherosclerosis. Excision of such a peripheral aneurysm with insertion of a graft is therefore a procedure which may be expected to be successful. We have resected a syphilitic popliteal

aneurysm with replacement by an infant's aorta with success[35] (Fig 445). Atherosclerotic aneurysms of the femoral and popliteal arteries should be replaced by grafts if the wall of the parent vessel is not excessively diseased. Successful resection of a mycotic aneurysm with replacement by a graft has been reported[36] Traumatic aneurysms are often suitable for grafting.

4. Occasionally removal of a segment of major artery is necessitated during the course of an operation, *e.g.* for removal of a carotid body tumour, radical neck dissection or involvement of a vessel in growth.

Technique of artery grafting.—The main vessel is dissected well clear of the obstructed or aneurysmal segment above and below, and the adventitia is cleaned off the vessel about the site of the proposed section. The artery is divided below, and if retrograde bleeding is free, and the wall healthy, a clamp, previously placed in position, is tightened to control bleeding. The clamp we prefer for this purpose is Potts patent ductus clamp as it does not slip, and does no damage to the artery, often atherosclerotic. Alternatively a rubber tube tourniquet can be used. The diseased artery is dissected up and divided across above the segment to be removed, a Potts clamp or other temporary control having been applied. A suitable graft is *chosen.* It should be a little smaller in diameter than the host vessel, as some dilatation will occur when it is subjected to intraluminal arterial pressure. Inequality of graft and host may give rise to turbulence of flow; this encourages intravascular thrombosis *The blind end* of the clamped patent vessel is washed out with heparin solution, as is the graft Three everting sutures, of 00000 silk, or 0000 silk in aortic grafting, on arterial needles are inserted, triangulating the vessels to be anastomosed; the *ends* are left long. One suture is then used to complete one third of the anastomosis, and this is tied to the suture which has been left long a third of the way around the circumference The next segment is similarly sutured until the anastomosis is complete The upper *anastomosis* is completed in a similar way, with the graft under sufficient tension to maintain it without tortuosity [illegible]

[illegible] they are kept covered for a few minutes with a sponge, they soon cease to bleed Sometimes an extra suture may have to be inserted. If the graft is done in a child interrupted *sutures must* be used to allow for circumferential growth Mattress sutures are best avoided, as not only do they have a tendency to constrict the lumen, but also a possibility of the fine stitches cutting out, the bite of tissue being very small.

Anticoagulants.—After the insertion of grafts for *trauma,* anticoagulants are probably *unnecessary.* When grafting has been done for diseased peripheral vessels, we heparinize the patient for twenty-four hours It has been found advisable to leave the wound of approach to the vessel approximated by one or two skin stitches only, in order that any bleeding

may escape to the surface rather than infiltrate extensively within the tissues of the limb. A delayed primary suture is carried out the following day.[44] Recently we have continued tromexan therapy for four weeks after grafting operations as it has been shown that prolonged therapy with this drug results in liquefaction of arterial thrombi produced experimentally.[37]

Within the abdominal cavity, anticoagulants are not used. Limited exercise in bed is allowed after five days, and the patient is allowed up after fourteen days.

AORTIC AND ILIAC GRAFTING.—Exposure of the aorta is by a long left paramedian incision from the costal margin to the pubis. When the lower end of the graft has to be joined to the external iliac artery, a "hockey-stick" incision with the horizontal limb dividing the rectus muscle is of great assistance. Care must be taken not to divide the inferior epigastric artery, a useful collateral in case of failure of the graft. The peritoneal cavity is opened in the same line. The splenic flexure, descending and pelvic colon are mobilised by incision through the parietal peritoneum in the left paracolic gutter, the ureter is dissected off the peritoneal leaf and left on the posterior abdominal wall, without disturbing it more than is necessary lest its blood supply be threatened.

The inferior mesenteric artery can be sacrificed if necessary and should be ligated near its origin from the aorta; it may be already thrombosed Great care is necessary in dissecting structures off an aneurysm, but a plane of cleavage is generally found, except where the aneurysm is in contact with the inferior vena cava. The extent of the aorta to be resected is defined, and the upper limit reviewed. There must be sufficient patent aorta below the origin of the renal arteries to provide a workable cuff of aorta and if this is less than 5 mm there is danger of thrombosis of the renal arteries. Rubber tourniquets are carefully worked around the aorta above, and the aorta or iliac vessels below Pott's clamps are then applied to occlude the lumen of the vessels above and below. The lumbar arteries in relation to an aneurysm are usually thrombosed and do not require ligation

The chief technical difficulty is the frequent close adherence of the aorta to the inferior vena cava, making dissection exceedingly difficult and tedious It is probably unnecessary to remove any more of the sac than is convenient, though sepsis and even osteomyelitis of the vertebrae has been reported when portions of sac have been left behind.

After removal of the aorta, the graft is inserted and sutured in position as previously described.

ARTERIO-VENOUS FISTULA

Traumatic fistulae.—Unless performed immediately after the injury, operation for traumatic arterio-venous fistulae should if possible be delayed for three months or more, for the following reasons :—

1. Many fistulae close spontaneously and some small fistulae produce no symptoms.
2. To enable the collateral vessels to enlarge as much as possible.
3. To allow the tissues around the fistula time to resolve after their reaction to the trauma, the sepsis and the haematoma which are usual about the injured vessels.

Early operation may rarely be necessary on account of increasing cardiac distress and increasing tachycardia.

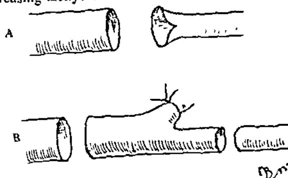


FIG 446
The vessel with the smaller diameter may be enlarged by an incision as indicated (A) Far better is the use of a branching graft (B).

After the application of a tourniquet the site of the fistula must be exposed widely, so that the vessels, both the arteries and the veins, above and below can be clearly dissected and temporarily ligated. The exact site of the fistula may be difficult to locate, but it will usually be found to be in the neighbourhood of :—

1. The site of maximum thrill
2. The precise point which when compressed results in slowing of the pulse rate (Branham's sign).
3. The position at which the proximal dilated artery gives place to a normal sized artery. The vein is hypertrophied above and below the fistula.

The fistula is then exposed by careful dissection. If there is a traumatic aneurysm as well, one or more nerves may be very closely associated with its wall, and if accidentally divided must be sutured.

METHODS OF TREATMENT OF THE FISTULA —If circumstances are such that there is a narrow fistulous connection, readily demonstrated, and of sufficient length then it can be ligated with a thick silk ligature. It would be preferable to divide it between ligatures but this is not often possible More probably the fistula is too wide for ligature, and in these circumstances the vein should be incised and the fistulous opening examined. It may be possible to suture the opening in the artery via the vein, reinforcing the suture line by folding and stitching the vein wall in layers, and then removing any surplus vein.

If this is impossible, then excision of segments of the artery and vein together with the fistulous tract should be done. After this, if practicable, a suitable graft should be inserted to bridge the deficiency in the artery, but enlargement of the artery proximal to the fistula may result in considerable discrepancy in size, and special methods of suture have then to be used (Fig. 446). The artery proximal to the fistula is often so friable that suture is difficult, and ligature precarious if amputation is demanded. Proximal ligation of the artery is not allowed ; it is nearly always followed by gangrene.

In patients with long-standing arterio-venous fistulae, the cardiac condition may be so severe as to make operation hazardous. Ligature of the vein proximal to the fistula may so improve this that operation on the fistula becomes safer.

Congenital fistulae.—Direct surgical treatment of the fistula, or fistulae for they are usually multiple, is seldom possible. If essential it is done in stages. Proximal ligation of the main artery does not affect the condition, and the frequently associated varicose veins are better treated by support only

ANEURYSM

Excision of the aneurysm and restoration of the arterial pathway by a graft is now the method of choice and well established practice Not every aneurysm can be so treated, and it is therefore necessary to evaluate the collateral circulation before surgery, as restoration of continuity may be impossible.

Matas' test still appears to be the most reliable method of estimating the collateral circulation[58] and Shumacker's modification appears to be usually satisfactory.[59] Ischaemia in the limb is produced by a sphygmomanometer cuff and maintained for five minutes. The artery to be ligated is then obstructed by the finger and the cuff released. If a good flush extends to the digits within two minutes, then the collateral circulation is considered adequate. The fallibility of the test arises from the difficulty of applying pressure to obstruct the main artery at precisely the point of subsequent occlusion Obliteration of a nearby collateral may result in diminished flush ; rarely does the test indicate a collateral circulation which is not available In those in whom the test indicates an insufficient collateral circulation, operation should be delayed until the effects of measures to increase this have been taken. Sympathectomy and repeated pressure on the aneurysm to the point of obliteration maintained until numbness or pain intervenes both assist the development of this. Embolic incidents after compression of an aneurysm are rare, and do not constitute so great a risk as might be expected.

When an aneurysm forms after arterial injury, operation should be delayed for three months or more to allow full development of collateral vessels and to give time for the surrounding tissues to resolve and condense *after* the injury and possible infection. Early operation may be necessary when there is rapid increase in size or pressure on neighbouring structures.

The aneurysm and the main vessels above and below are carefully dissected as nerve trunks may be closely adherent to the sac. The vessels are temporarily controlled, and the sac is excised, or if this is difficult, infolded and obliterated, and a graft inserted If it is considered that grafting is impracticable, the sac is opened with minimal dissection and with the circulation controlled by a tourniquet; by such means injury of collateral vessels is avoided. From within the sac all the entering arteries are closed by suture, and the sac in-folded by suture to effect complete obliteration.

P. M.

SURGICAL TREATMENT OF LYMPHOEDEMA OF THE LEG

The contributions of surgery to the treatment of lymphoedema have aimed either at a method of draining the limb or the ablation of the oedematous tissues. Drainage methods have been described by Handley[60] who implanted silk strands in the limb, Lanz[61] who used strips of fascia lata, Kondoleon[62] who excised strips of deep fascia in the belief that the fluid would be re-routed in the muscle planes, and Gillies[63] who transplanted lymphatic bearing flaps to act as a by-pass.

Many workers, including Charles[64] have advocated excision of the abnormal tissues of the limb, and the main controversy has centred around the techniques by which this may be done. Since Homans[65] described his procedure for radical excision many modifications have been suggested[66 67 68 69 70 71 72]

In this literature it will be seen that the main point at issue is the method whereby the limb is resurfaced after the excision has been done

Whatever be the sequence of events which may predispose to the condition of lymphoedema, it is the inexorable hydrostatic pressure which favours the progress of the disease In planning treatment the effect of gravity must be given first consideration and it is this factor which militates against any form of drainage operation

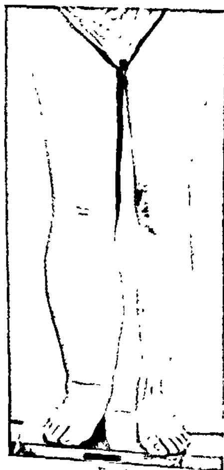


FIG. 447
Lymphoedema praecox

It would appear that the primary pathology is confined to the lymphatics of the subcutaneous tissues, for oedema of the muscles is not seen in idiopathic

lymphoedema although it may be present in lymphoedema secondary to chronic venous insufficiency. The lymph-sodden tissues become enmeshed in fibrous tissue and the deep fascia and the skin may be affected. Once fibrosis has made its appearance the process is irreversible and the swelling becomes progressively more solid (Fig. 447).

From these considerations operative treatment should be designed to remove completely the abnormal subcutaneous tissues of the limb, the deep fasciae where they are thickened and contracted, and to resurface the defect with full thickness skin. The upper limit of the excision is usually below the knee but may be carried up on to the thigh. The sole of the foot is left intact and the toes are not interfered with at this operation but may be reduced in size at a later date. At the upper end the transition is not left as an abrupt line but the integument should be reduced to form a cone so as to produce an acceptable contour. Unless this refinement is added an unfortunate " plus-fours " effect will result In above-knee reductions the popliteal fossa is not uncovered except in gross cases when the skin is lifted as a flap and returned to its position after excision of the oedematous tissue.

In view of the extent of the operation careful choice of case is necessary.

The length of history, the size of the limb and the patient's reaction to his deformity must be carefully assessed. Intelligent co-operation after surgery is essential to success and it is wise to examine the patient on more than one occasion before the decision to operate is made.

A week to ten days' rest in bed with the limb elevated to 45° in a Thomas splint is the routine. This period is required to drain the excess fluid. It makes the dissection much easier and the tourniquet applied prior to operation remains tight throughout the procedure. Daily friction and deep massage together with exercises in elevation are used to promote the circulation and to improve the quality of the skin which will later have to survive as a graft.

Special attention should be paid to the toes where fungus and other infections not infrequently lurk. In patients who exhibit infective interludes, a quiescent period should be chosen and prophylactic penicillin cover is probably wise. A high protein diet is encouraged from the day of admission and is continued until healing is well established.

A simple method of holding the limb elevated is by making a bridge between two lithotomy poles with a bandage and then adjusting the patient's position on the table so that the point of the heel rests on the bandage sling. A sterile Esmarck tourniquet is applied after the skin has been prepared, diathermy connections are made, and the operation area is towelled off.

The incision, which is marked in Bonney's blue, passes round the leg at the level of the tibial tuberosity and in the posterior mid-line descends vertically down to a point just above the malleoli. Here it divides to leave a narrow triangle of skin over the Tendo Achilles and skirts the lateral and medial borders of the foot to the toe webs where the two incisions meet.

The skin together with all the subcutaneous tissue is then dissected off the leg, starting at the knee where the fat is coned down to the level of the deep fascia. The saphenous veins and the superficial nerve trunks are sacrificed. Particular care is taken to remove all the tissue behind and above the malleoli. On the dorsum of the foot and ankle the paratenon should be left intact over the extensor tendons (Fig. 448).

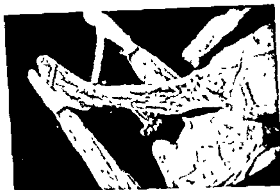


FIG 448
Position at operation and dissection completed. The leg is held in elevation on a bandage sling between two lithotomy poles.



FIG. 449
The fat is stripped off the excised mass.

If any part of the deep fascia is observed to be much thickened it should be excised The tourniquet is removed and an assistant is made responsible for haemostasis Major vessels are ligated with 3/0 catgut and minor bleeding points are diathermised Fifteen to twenty minutes may elapse before the wound is dry The massive specimen is taken to a side table where the fat is split off from the skin. This may be done by making parallel incisions half-an-inch apart through the fat down to the level of the dermis and cutting each fat strip off with curved scissors or a knife. An alternative method is to

divide the whole specimen into three longitudinal parts of equal width and split off the skin, using a Humby knife. The three skin strips are then sewn together before re-application to the leg (Fig. 449).

Whichever method is used it is essential that all fatty remnants shall be removed from the skin as areas of necrosis will result from their presence.

When the skin has been replaced there will be an excess in all dimensions which should be trimmed away until a glove-fit under normal skin tension is obtained. Too little tension is to be avoided as it seems to be one of the causes of dyskeratosis which sometimes occurs in these big grafts.



Fig 450
The same limb as in Fig 447 after operative reduction

The graft is then sewn in accurately round the foot and knee but sutures are sparingly used in the long posterior incision as it is here that drainage is to be encouraged

A line of half-inch stab wounds is made through the skin down the antero-lateral and antero-medial quadrants of the leg to assist drainage from these parts. Tulle gras is then applied over the graft and "Orthoban" wool strips wrung out in saline or flavine emulsion are carefully moulded to the surfaces, particular care being given to the region round the malleoli The wool mould should be built up evenly so that uniform pressure from the bandages will be transmitted to the graft. The dressing is then secured with crepe bandages at a pressure just below that which will cause congestion in the toes and a plaster back-slab completes the fixation

The leg should remain in elevation at 45° during transfer from the theatre to the ward and at no time during the first ten days should it be allowed down.

In the tenth day the dressing is done and any doubtful areas of the graft noted By the fourteenth day it will be obvious if some of the skin has not survived, and at this time the patient should be returned to the theatre for localised excision of the necrotic areas and grafting with split skin from the same thigh. This is a time-saving measure as slough sequestration in these cases is a slow process.

In the successful case bed exercises are started during the second week and walking is allowed the week after. Supervised exercises should be continued to encourage the circulation, and to regain joint function. Great advantage is to be gained by skilled nursing care of the grafted skin which should be kept free of debris, serum and exudates.

On discharge from hospital the patient should wear elastic bandages for three to six months, and the daily application of lanoline with light friction massage assists in the consolidation of the new skin. This can be managed by most at home (Fig 450). J. N. B

ANAESTHESIA IN PERIPHERAL VASCULAR SURGERY

General anaesthesia is required for most major procedures in peripheral vascular surgery and is also employed to make arteriography easier for the patient and more convenient for the radiologist. It is the purpose of this section to discuss the management of general anaesthesia in these circumstances

Regional blocks are used in peripheral vascular surgery as therapeutic measures or for investigative procedures. The appropriate techniques are described elsewhere in this book.

Many new developments in peripheral vascular surgery are directed at specific local manifestations of generalised arterial disease. In such patients a history of *previous* cardiac and cerebral incidents is not uncommon and it is undoubtedly true that in this group the danger of sudden catastrophe is real

In the pre-operative assessment of these patients electrocardiographic examination is of considerable assistance to the anaesthetist, often revealing unsuspected evidence of coronary insufficiency. It is important to realise that such complications are not confined to patients undergoing major surgery but may also occur in the routine investigation of disease under anaesthesia. The anaesthetist, therefore, should regard anaesthesia for arteriography as a procedure carrying risks comparable with those of major surgery.

[illegible] majo [illegible] the intra-arterial injec[illegible] of a contrast medium is a painful procedure, such investigations are usually carried out under general anaesthesia. Moreover, general anaesthesia, by producing peripheral vasodilatation, enables the medium to be distributed more effectively.

As arteriography is normally carried out in the presence of X-ray equipment, the use of explosive anaesthetic agents is excluded. A thiopentone induction with maintenance by nitrous oxide and oxygen is pleasant for the patient and free from explosive risk. Very light anaesthesia, however, is unsatisfactory and it may be necessary to supplement with intravenous pethidine or, if preferred, minimal doses of trichlorethylene.

Abdominal aortography is performed in the prone position and in these cases endotracheal intubation is indicated to ensure a clear airway at all times during the investigation. The introduction of the short-acting relaxant succinyl choline has greatly facilitated intubation during light anaesthesia, adequate relaxation being readily obtained with a dose of 50 mg. given intravenously.

Endotracheal anaesthesia is also indicated for carotid angiography and here the use of an armoured tube is advisable to protect the airway during the various changes of position often necessary for satisfactory films. When bilateral carotid angiography has been carried out it is frequently wise to leave the endotracheal tube in position until it is certain that obstruction from haematoma formation has not occurred.

Anaesthesia for major surgery.—Major surgical intervention in peripheral vascular disease may be directed at the nervous control of the vascular system or alternatively at the site of the disease in the vessels themselves. Where the disease involves main trunks such as the aorta, surgery has been limited until recently by the fact that occlusion of the aorta for even a brief period tends to produce irreversible changes in the spinal cord. Experimental work in dogs has shown that hind quarter paralysis may follow temporary occlusion of the thoracic aorta.[73] It has however been demonstrated that hypothermia will protect the cord against temporary anoxia.

Hypothermia.—*The application of hypothermic techniques to clinical* surgery has led to considerable advances in the treatment of aortic disease. Induced hypothermia by reducing the metabolic rate and consequently the *tissue demands for oxygen, now enables the surgeon to occlude the aorta for* long periods without danger of tissue anoxia.

Electrocardiographic control is essential for the proper management of induced hypothermia and the method should never be used in its absence. Spontaneous ventricular fibrillation is a constant hazard of the technique and the electrocardiograph is absolutely necessary for its early detection. This, of course, implies that the surgeon must always be prepared to open the chest and apply a defibrillator directly to the heart.

There is no absolute contraindication to the use of hypothermia but it should be remembered that elderly arteriosclerotic patients do not readily make the necessary circulatory adjustments imposed on them by the nature of the surgery.

Before satisfactory cooling can be achieved it is essential to prevent any stress reaction—the normal response to cold. If this is not inhibited the cooling effect is slowed and may even be reversed, and in addition the patient is exhausted. Premedication is important in this respect and Beard[74] recommends the administration of 25 mg. of promethazine by mouth the evening before, followed by 50 mg. by mouth four hours before the operation is due to begin. In addition, 100 mg. of pethidine is given intramuscularly an hour

before induction. The simplest criterion of the onset of the stress reaction is the degree of shivering and it should be the aim of the anaesthetist to prevent this by the adequate use of relaxants. Cooling is further facilitated by peripheral dilatation, a state readily obtained by the induction of general anaesthesia in any form

It has been stated that the method used to produce hypothermia is not of great importance but that, of the means available, surface cooling is the simplest and possibly the safest[75] The technique of blood cooling described by Delorme[76] involves the establishment of an artificial arterio-venous fistula and is not recommended for patients suffering from peripheral vascular disease.

Surface cooling may be achieved by the immersion of the anaesthetised patient in ice-cold water or by the frequent application to the whole body surface of towels wrung out in ice-cold water. These techniques are not very practicable and the most convenient method of cooling is to place the patient on a rubber mattress through which a rapid flow of cold water is maintained.[77]

After the induction of anaesthesia with intravenous thiopentone a suitable dose of tubocurarine sufficient to paralyse respiration is given intravenously and the patient is intubated. Anaesthesia is maintained with a 50 per cent. mixture of N_2O and oxygen. Cooling is then begun and is continued unitl the body temperature falls to 30°C. at which level the procedure is ended and the patient is transferred to the operating table. Cooling to this extent may take sixty to ninety minutes and is partly dependent on the patient's physical build. A further fall in temperature of two to three degrees is to be expected after the operation is begun This after-drop is greatest when the pleural cavity is opened, though exposure of the abdominal contents also influences the degree of heat loss

Nitrous oxide is the most satisfactory agent for the maintenance of anaesthesia During hypothermia body metabolism is low and drugs are detoxicated extremely slowly. Consequently agents such as thiopentone and pethidine exert a prolonged effect even in small doses and are better avoided. Moreover, these drugs have a central depressant effect on respiration which, if severe, must inevitably lead to carbon dioxide retention, and as the solubility of carbon dioxide in the plasma is increased at low temperatures this risk is considerably greater in the hypothermic patient than in the normal. The anaesthetist, therefore, must ensure that controlled respiration is ventilating the lungs adequately

Particular care is required in the administration of intravenous fluids during hypothermia Because of the general depression in metabolism glucose is not removed from the blood as rapidly as under normal conditions so that, if glucose-saline is given indiscriminately, there may be a marked elevation of blood sugar

Although the principal advantage of hypothermia is the reduction in tissue demand for oxygen there are other benefits for the surgeon. The technique provides an almost bloodless field which facilitates the surgical

approach. Furthermore, the slow heart rate and the reduced pulse pressure combine with a fall in cardiac output to present the surgeon with nearly ideal operating conditions for surgery of the large vessels.

Controlled hypotension.—Thoracolumbar splanchnicectomy and sympathectomy is an extensive operation involving the separation of many tissue planes. The provision of a bloodless field is of considerable assistance to the surgeon in this type of operation, and for this purpose Griffiths and Gillies[78] introduced total spinal analgesia. This technique implies, as the authors state, a total sympathetic block with lesser degrees of sensory and motor paralysis, designed to effect the maximal fall in blood pressure leaving the muscles of respiration and the medullary centres unaffected. Because the sympathetic outflow is blocked the vagal effect is predominant and the pulse rate slows to a rate of 50 per minute or less. The blood pressure falls to a level of approximately 50 mm. Hg or lower, the cardiac output is reduced and the pulse pressure correspondingly falls.

A suitable dose of morphine and atropine is given as premedication an hour before the operation is due to begin. In the anaesthetic room the patient is given 0·5 g. thiopentone intravenously followed by 50 mg. of succinyl choline by the same route. The larynx is then exposed and sprayed with 2·0 per cent. amethocaine. Intubation is carried out and anaesthesia is maintained with a 50 per cent. mixture of nitrous oxide and oxygen. Respiration is controlled until normal breathing returns. At this stage the patient is placed in the lateral position and lumbar puncture is performed in the third lumbar space Procaine 150 - 300 mg. is dissolved in a 3 - 5 ml. of cerebro-spinal fluid and injected intrathecally. The patient is returned to the supine position and the operating table is placed in a steep Trendelenburg which is maintained until an adequate fall in blood pressure occurs The position of the patient can then be modified to meet the requirements of the surgeon but it is emphasized that a limited head-down position is essential when this technique is employed.

With procaine the hypotensive effect lasts for approximately thirty minutes If a more prolonged effect is required 1·5 - 3 ml. of 1 . 200 heavy cinchocaine should be used instead of procaine for the intrathecal injection

Animal experimental work has shown that the fall in blood pressure which results from total spinal block is associated with a reduction in oxygen consumption of approximately 20 per cent. below the normal anaesthetic level.[79] Further work suggests that this fall in oxygen consumption is due to a diminution in the tissue demands for oxygen and not to a reduction in the supplies available.[80] Total spinal analgesia may be an excellent alternative to hypothermia for surgery of the large vessels.

The management of total spinal analgesia is not easy As peripheral pulses may be absent and the blood pressure unrecordable the assessment of the patient's condition is usually made on the rate and depth of respiration together with the general appearance and absence of cyanosis If, however,

the pleura is opened respiration must be controlled and the criteria are more limited. Under such circumstances electrocardiographic control is most valuable and should always be available.

Patients submitted to controlled hypotension tolerate haemorrhage badly. For this reason an intravenous infusion should be established before the operation is begun so that blood loss may be replaced as it occurs. Occasionally it may be necessary to give blood rapidly if haemorrhage is severe, and a hand pump of the type described by one of us[41] is recommended for this purpose.

The hypotensive state may be reversed by the intravenous injection of amphetamine 10 - 30 mg. Its use is indicated if cyanosis develops and persists despite adequate ventilation with oxygen.

Severe anaemia and aortic valvular disease are perhaps the only absolute contraindications to total spinal analgesia, but a history of coronary thrombosis should suggest the use of another technique.

Other hypotensive methods have been used for sympathectomy but in the author's opinion neither the methonium compounds nor arfonad can offer the same safety in action combined with certainty of effect as total spinal block.

Routine general anaesthesia.—Cervical sympathectomy *presents very little* problem for the anaesthetist provided the patient is intubated. Intubation, preferably with cuffed tube, is advisable as the pleura may be opened during the dissection, making it necessary to control *respiration*.

In operations where no special anaesthetic technique is required, the method described by Brennan[42] in 1952 is recommended After induction with thiopentone the patient is given a suitable dose of relaxant and intubated. Hyperventilation with 75 *per cent.* nitrous oxide and 25 per cent. oxygen is carried out for the following ten minutes by which time a satisfactory level of analgesia is obtained. Thereafter the patient is maintained on this mixture for the duration of the operation Occasionally anaesthesia may have to be supplemented by small doses of intravenous pethidine.

Anaesthesia for out-patients.—In the radical treatment of varicose veins, the general shortage of hospital beds combined with the large number of patients requiring operation has forced many surgeons to undertake this as an out-patient procedure. The *dissection* of varicose veins may take some time and the anaesthetist must be prepared to provide prolonged anaesthesia. At the same time, recovery must be rapid to allow the patient to be *discharged* from hospital the same day This can best be achieved by a combination of local and general anaesthesia.

Lignocaine is a satisfactory local anaesthetic and approximately 80 - 100 ml of 0 5 per cent solution are required Two wheals are raised, one just medial to and *below* the anterior superior iliac spine and the other just lateral to the pubic tubercle. Through these wheals the skin and subcutaneous tissue

are infiltrated for four inches downwards on the lateral and medial aspects of the thigh and the wheals are connected by a similar infiltration above the inguinal ligament. Immediately lateral to the femoral artery and below the inguinal ligament 20 ml. of solution are deposited below the deep fascia in the region of the femoral nerve, and finally the lines of incision are infiltrated. When the dissection is complete a mixture of 80 per cent. nitrous oxide and 20 per cent. oxygen is administered for the procedure of stripping. Recovery of consciousness occurs rapidly, with the minimum of inconvenience.

J. P. P.

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tympani is usually reported by the patient not as a loss of taste in that region, such as presents itself when the stretched-out tongue is tested, but usually rather as a falsification of taste, because the patient can still perceive the finer flavors of food through the olfactory system while the perceptions of acid, salty, bitter and sweet are absent. The result is a peculiar distortion, rather than loss, of the perception usually referred to by laymen as "taste."

In parkinsonism and other extrapyramidal disorders, *loss of spontaneous mimic facial expression* (amimia) occurs, usually associated with prolonged course of elicited mimic responses. Extrapyramidal rigidity and adiadokokinesis of facial movements not necessarily connected with obvious amimia can be tested by the whistle-smile diadokokinesia, i. e, by testing the speed with which the patient can alternately whistle and smile. Hanes has called attention to the fact that most normal patients when asked to whistle will follow this act by a spontaneous smile which he claims is absent in extrapyramidal disorders, especially parkinsonism.

A rare but significant finding is dissociation of the ability to perform voluntary facial movements from that of involuntary emotional facial innervation. This type of dissociation usually points to a deep-seated cerebral lesion, especially striatal or thalamic. Fig. 539 shows a patient who presented this type of dissociation. Fig. 539*A* shows the patient's face at rest. Fig. 539*B* shows voluntary innervation which is symmetric in spite of a certain apraxia-like clumsiness. Fig. 539*C* shows the patient with a spontaneous smile; it is seen that only the left side smiles while the right does not.

VIII: Eighth Nerve

The eighth nerve is divided into the cochlear (auditory) and the vestibular (equilibratory) portion.

Cochlear Portion. A preliminary impression as to the integrity of this portion can be obtained by determining the distance at which the ticking of a pocket-watch can be heard, the examiner can readily control the performance by his own ability to do so or by that of another normal person. Another simple test is to rub thumb and forefinger together a few inches away from the patient's ear. Middle-ear deafness affects chiefly low tones, nerve deafness, high tones A preliminary impression regarding that point can easily be gained by modulation of the examiner's voice, including the use of whisper and whistle. The more accurate examination which has supplanted the older elaborate set of tuning forks is the use of the audiometer which should be used whenever indicated.

The *Weber test* is difficult for most students to understand. The best clear-cut simple description is that given by Putnam: "If the middle ear is affected, sounds heard by bone conduction are relatively intensified. A tuning fork on the forehead or bridge of the nose is better heard in the deaf ear if the middle ear is chiefly involved, less well if the nerve is involved. If no tuning fork is at hand, a watch laid on the mastoid may serve for differentiation."

Vestibular Portion. Excitation of the vestibular system (labyrinth, vestibular nerve or vestibular nuclei in the medulla oblongata) of one side produces nystagmus toward the same side and tonic phenomena (past pointing and falling or veering) toward the contralateral side. In

mus after its quick component, which is actually not the primary one, but merely the quick jerking back after the slow component—the primary one—has had its run. It is obvious therefore that the slow tonic component of the nystagmus, which is its true primary component, goes toward the same side as the other tonic phenomena, i. e., to the side opposite to the labyrinth or vestibular nerve or nucleus stimulated.

It is furthermore important to keep in mind that the impulses generated by either vestibular system, unlike those coming from other sensory systems, are continuous and rhythmic, each side being normally in bal-

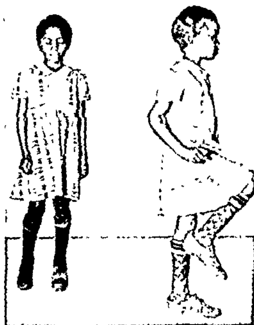


Fig. 540 (Patient No. 6.) Mittelmeyer's test, positive in a case of predominantly left-sided vestibular degeneration in a non-albinotic girl coming from a family with frequent incidence of albinism (From F Schnoor and E T. Thompson)

ance with the other, like two reins held with even force by a steady hand. Therefore destruction or impairment of the vestibular system of one side causes nystagmus and tonic phenomena only by giving the preponderance of continuous innervation to the other side. The resulting directions of nystagmus and tonic phenomena after destruction or impairment of one vestibular system are identical with those which could be produced by excitation of the other vestibular system. Accordingly, destruction or impairment of one vestibular system produces nystagmus toward the contralateral side and tonic phenomena (past pointing and falling or veering) toward the same side.

In order to determine whether any particular set of spontaneous vestibular phenomena is due to excitation of one or due to destruction or

nerve. Bilateral involvement of the vagus system, such as the bilateral involvement of the pneumogastric (dorsal) nucleus of the vagus in Wernicke's disease, causes, among other disturbances, marked tachycardia.



Fig. 541. Radicular paralysis of left hypoglossal nerve Note that the tongue is pushed out toward the paralyzed side, withdrawn toward the normal side (From Dinkler)



Fig 542. Malingerer (patient No. 8) Tongue is pushed out to the left, but without bulging prominence. (Courtesy of Dr. R. S. Lyman)

It is useful to know that the anterior aspect of the external auditory canal receives its sensory innervation from the vagus nerve.

impairment of the other vestibular system, testing is necessary. The procedures are well described in the standard otoneurologic texts: special reference is made to Alexander, Marburg, and Brunner's Handbook, to Spiegel and Sommer's Ophthalmo- and Oto-Neurology, to Grahe's brief compendium, and to the books by Camis, Ballenger (see also Chapter VI, p. 207) and Turner. The most important tests are the caloric examination, the examination in the turning chair, and the galvanic examination.

For the general practitioner or the neuropsychiatrist the *caloric examination* will usually suffice. Thirty to one hundred cubic centimeters of *warm or cold water respectively* may be used and irrigated into the outer ear. The warm water used should never exceed 48° Centigrade. After irrigation with warm water the nystagmus and tonic phenomena are identical with those which would result if that same vestibular system were stimulated; after irrigation with cold water they are identical with those which would result from inhibition (temporary destruction or impairment) of that same vestibular system. In other words, irrigation of the normal ear with cold water produces nystagmus to the other side, tonic phenomena (past pointing and falling) to the same side, while irrigation with warm water produces nystagmus to the same side, tonic phenomena to the other side.

A special sign known to otologists as *fistula symptom* may be important to neurologists because it occurs occasionally without the presence of a fistula in cases of congenital syphilis. This sign consists in the abnormal *elicitability of nystagmus and tonic phenomena, either by injection of air* at room temperature into the external auditory canal, or by withdrawal of air by suction from it. In the presence of a fistula between labyrinth and middle ear, or in cases of congenital syphilis without such fistula, injection of air will act like stimulation, aspiration of air like temporary destruction of that labyrinth.

A good test for slighter degrees of tonic phenomena such as veering is that described by Mittelmeyer. If the patient is asked to "march" without progression on one spot, the patient suffering from abnormality of the vestibular system will gradually turn to the side contralateral to vestibular excitation, or homolateral to vestibular loss (Fig. 540).

It is well to emphasize at this point that the vestibular system is interlinked with cerebellar, mesencephalic, diencephalic, frontal and temporal systems, and the unraveling of the primary seat or seats of the disturbance requires thorough, ingenious and systematic correlation of all data obtainable.

IX: Glossopharyngeal Nerve

The outstanding readily tested function of this nerve is taste over the posterior third of the tongue.

X: Vagus Nerve

The outstanding symptoms of unilateral impairment or loss of the vagus nerve are hoarseness of voice, difficulty in swallowing and paralysis of one-half of the velum palatinum. The latter symptom may occasionally be absent, because in rare cases the fibers from the anterior tip of the nucleus ambiguus which innervate the velum palatinum leave the medulla oblongata not with the vagus nerve such as is usually the case, but atypically with the facial

should be supplemented by an electrical examination Two types of currents may be used, faradic and galvanic current. With the *faradic* current the presence of reaction, its promptness, quality and duration, especially the presence or absence of lingering contraction, such as that obtained in myotonia, may be ascertained. The *galvanic* test should be used to measure threshold values and to determine the presence or absence of quantitative reduction or of reaction of degeneration.

In *quantitative reduction,* such as that which occurs in certain muscular diseases and degenerations, the threshold of nerve and muscle stimulation is simply raised. In *degeneration* of the nerve, if it is complete and of long standing, no reaction at all can be elicited by stimulation of the nerve, while direct stimulation of the muscle, if any muscle fibers are still preserved at all, will produce a slow wormlike contraction. The acute

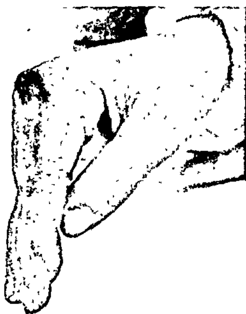


Fig 543 (Patient No. 9) Posture of hand in Parkinson's disease (Courtesy of Dr R S. Lyman)

and subacute *reaction of degeneration* is due to degenerating (not completely degenerated) lower motor neurons. Its outstanding sign is an inversion of cathode and anode thresholds on the basis of Pfluger's law, which for purposes of practical clinical examination can be reduced to a very simple formula· Normally, stimulation thresholds by means of the anode are about twice as high as stimulation thresholds by means of the cathode. In reaction of degeneration this relationship is either reversed, or, in cases of incomplete reaction of degeneration, reduced, that is, in incomplete reaction of degeneration cathode and anode thresholds become approximated to each other, i. e., identical or similar. In complete reaction of degeneration the anode thresholds become lower than the cathode thresholds. Furthermore, in reaction of degeneration, the contraction of the muscles is slow and wormlike, but this cannot always be

XI: Accessory Nerve

This nerve supplies the motor innervation of the sternocleidomastoid and trapezius muscles.

XII: Hypoglossal Nerve

This nerve supplies the motor innervation of the muscles of the tongue. It is not generally remembered that in unilateral paralysis of the hypoglossal root or nerve the tongue is pushed out toward the paralyzed side, but withdrawn toward the healthy side (Fig. 541); Dinkler pointed out this fact in 1898 in his still classical paper. Another important fact pointed out by Dinkler is that in the acute stage of hypoglossal paralysis the paralyzed side of the tongue appears higher and more voluminous, until atrophy supervenes. Atrophy, however, does by no means occur in all cases of peripheral hypoglossal paralysis because recovery may occur before atrophy has set in. This bulging prominence of the paralyzed side of the tongue which Dinkler described in infranuclear palsies was found by Lyman to be present also in supranuclear hypoglossal palsies. In hysteria or malingering this bulging deformity is absent (Fig 542).

NECK, TRUNK AND EXTREMITIES

After examination of the cranial nerves, the neurologic examination concerns itself with neck, trunk, and extremities

Strength and Tonus

Strength. The method of examination of strength in the various muscle groups of neck, trunk, and extremities is obvious, provided one is familiar with their special functions and directions of pull. The beginner should always consult a good textbook of anatomy which gives special attention to muscle and nerve function. Quantitative data for the strength of the hands can be obtained by the use of the dynamometer, but for neck, trunk, arms and legs, reliable methods of quantitative measurement have not been successfully devised; here we still have to rely on a rough quantitative estimate In estimating the strength of the legs, for instance, the most reliable test is still the ability of the patient to carry his weight while standing and walking. Especially in powerfully-built and muscular men direct manual examination on the examining table will usually fail to demonstrate a subtle or moderate degree of loss of strength even if it is significant enough to be demonstrable beyond any doubt by disturbance of the patient's ability to carry his own weight in standing or walking. After all, we measure the strength of legs on the examining table with our arms which are no adequate measure for the amount of strength which a muscular and powerfully-built man can deploy in his legs even though his strength may be significantly reduced. If the reverse is the case, i. e., if a man can carry his weight and stand and walk but when placed on the examining table demonstrates a degree of weakness of his legs measurable with the examiner's arms and hands, such a patient is invariably a suspect of hysteria or malingering unless he may be suffering from a more complicated form of apraxia which does not involve stance and gait, but does involve other voluntary movements.

Electrical Examination. The mechanical examination of strength

clinical tetanic states the characteristic tetanic posture of the hand may be brought about by applying a blood pressure cuff to the arm sufficiently tight to interfere with venous return and arterial influx for a few seconds (Trousseau's sign).

In torticollis spasticus, the differential diagnosis between its extrapyramidal organic form and its hysterical conversion form taxes the in-



Fig 545 (Patient No 11.) Athetosis (Courtesy of Dr. R. S. Lyman.)

genuity of the most experienced neuropsychiatrists. Myographic records will almost always be necessary to make the differential diagnosis, although a few of the more superficial criteria may provide useful hints. In the extrapyramidal type of torticollis spasticus (Fig. 544*A*) the ability of the patient to turn the head toward the other side is usually limited (Fig. 544*B*); and when the patient is asked to open the mouth forcefully, there is usually only incomplete correction of the abnormal posture (Fig. 544*C*).

counted upon in cases of partial degeneration of the nerve, and therefore should not be regarded as an essential criterion of reaction of degeneration.

Tonus. In examination of the tonus, the sensitive hand of the examiner is still the finest instrument. Various tonometers have been devised, one by Spiegel, later ones by Schaltenbrand and others. A helpful maneuver for measurement of tonus of the arms is Babinski's phenomenon of exaggerated flexibility of the forearm against the elevated upper arm (see Figs. 573*A*, 574*A*, 575*A*). If there is reduction of tonus the forearm can be flexed against the elevated upper arm at an extraordinarily acute angle, while if there is an increase of tonus the angle will be more obtuse than normal. Similar







Fig 544. Torticollis dystonicus ("spasticus") extrapyramidalis (patient No. 10). *A*, Spontaneous posture *B*, Voluntary turn toward side opposite to habitual posture. *C*, Forceful opening of mouth on request (Courtesy of Dr R. S. Lyman)

maneuvers can be carried out with the legs. This change can be quite dramatic in extreme states of reduction of tonus, such as, for instance, in those prevailing in certain types of cerebellar disease.

Postures

Abnormal postures should be described carefully and, whenever possible, photographic records should be kept.

Among the more typical abnormal postures are the hypertonic hand with approximation of fingers found in Parkinson's disease (Fig. 543), the hypotonic overextended hand found in chorea and the characteristic posture of the hand found in tetany. It is well to remember that in sub-

Athetosis. Athetosis (Fig. 545), if limited to the extremities, may be defined as follows: location predominantly in distal parts of extremities; frequency slow; speed of individual movements rather considerable, more so than one would think in observing the total pattern; the impression of slowness of athetoid movements is in large part an illusion brought about by the tendency to maintain the limb in an extreme end position for con-

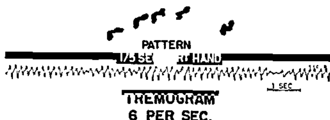


Fig. 547. (Patient No. 12) Tremor pattern record and tremogram in arteriosclerotic parkinsonism (Courtesy of Dr. R. S Lyman)

siderable time after the movement itself has been completed, thereby giving a slow wormlike appearance to the total pattern; no rhythm; there is a certain regularity of pattern and considerable uniformity in individual movements; amplitude variable, larger than in chorea, smaller than in ballism; force considerable. Athetosis, especially infantile athetosis, is seldom limited to the extremities, but usually torsion movements of neck

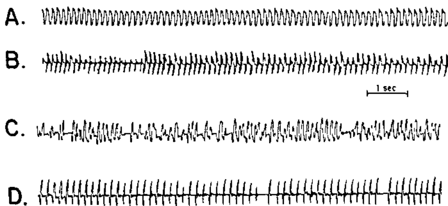


Fig. 548 *A*, Spontaneous tremor in Parkinson's disease (patient No. 13), kinetogram Rate 7 beats per second. Note regularity of pattern *B*, Tapping (diadokokinesis) in the same case of Parkinson's disease (patient No. 13) Rate 7–8 taps per second *C*, Spontaneous tremor in hysteria (patient No 14), kinetogram Rate 8–10 beats per second Note irregularity of pattern *D*, Tapping (diadokokinesis) in the same case of hysteria (patient No. 14). Rate 6 beats per second (Courtesy of Dr. R S Lyman)

and trunk occur as well (Fig 546); when the hyperkinesis of trunk and neck predominates over that of the extremities, the picture is usually referred to as *torsion dystonia;* but clinically as well as pathologically, athetosis and torsion dystonia belong to the same disease entity, differing only in somatotopic localization (L. Alexander, 1941)

Tremor. Tremor may be defined as follows· location predominantly in the distal parts of extremities; frequency rapid (in organic extrapyram-

Involuntary Movements

In involuntary movements it is important to describe the hyperkinesis in as simple terms as possible and according to a definite system, rather than to be satisfied with attaching a one-label diagnosis, which may not always be agreed upon by different observers. I have found description according to the following eight special criteria useful in describing the salient features of any hyperkinesis with sufficient essential detail to allow those who read the record to draw their own diagnostic conclusions. These eight essential features are: (1) location (distribution); (2) frequency (rate of the total hyperkinesis—"how frequent are the movements?"); (3) speed of the individual movement; (4) rhythm, or absence of rhythm; (5) regularity of pattern; (6) uniformity or multiformity of individual movements; (7) amplitude of movements; and (8) force of movements.



Fig 546 (Patient No. 11.) Athetosis (Courtesy of Dr. R S Lyman)

Chorea. According to these criteria, chorea, for example, may be defined as follows: location of movements predominantly in distal parts of limbs, although the proximal parts, trunk and face may participate to a lesser extent; the frequency is variable and rather slow; the speed of each individual movement is considerable; the hyperkinesis is nonrhythmic; the total pattern is irregular, and there is little uniformity of individual movements; the amplitude of the movements is small, and their force is feeble

Ballisms. Ballisms may be defined as follows: location predominantly or exclusively in proximal parts of limbs; frequency rapid; speed of individual movements rapid. There is a rather regular rhythm; the pattern is regular and the individual movements uniform; amplitude is large, and the force is great.

be elicited during or immediately after the attack, e. g., the positive Wartenberg in the electrically-induced convulsion shown in Fig. 549. The pattern of *opisthotonos* should always be described in detail. Opisthotonos

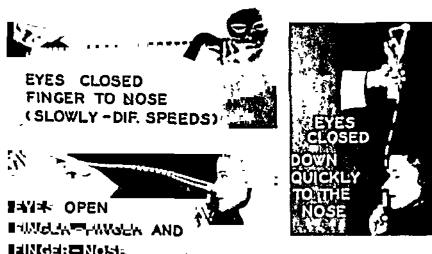


Fig 550. Tests for coordination of upper extremity. Normal individual (Courtesy of Dr R S Lyman)

caused by organic conditions, such as disease of the vestibulo-extrapyramidal system, e. g., in Wernicke's disease, or certain organic epileptic fits, is always due to violent contraction of the long muscles of neck and back;

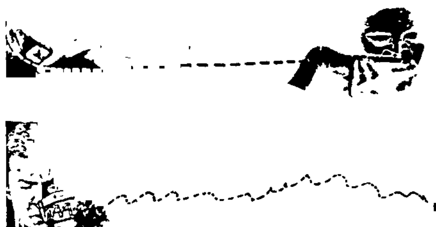


Fig. 551. Finger-to-nose test with eyes closed. Upper Normal individual. Lower: A case of multiple sclerosis with left-sided cerebellar symptoms (patient No 17). (Courtesy of Dr. R. S. Lyman)

in contrast to this an opisthotonos which receives support from the patient's elbows should always be suspected of being an hysterical "arc de cercle."

idal tremor about 6-8 beats per second); speed of individual movements considerable; strict rhythmicity; pattern extraordinarily regular, and individual movements uniform; amplitude and force of movements small. Fig. 547 shows a pattern record of *tremor by recording* the excursion of small lamps tied to the tips of the fingers of the trembling hand; this together with the tremogram (Morris) gives a very complete graphic record of the tremor.

Tremogram and tapping records allow a very clear-cut differential diagnosis between organic extrapyramidal tremor and hysterical tremor. ***Organic extrapyramidal*** (striatal or nigral) ***tremor*** usually runs about 7 beats per second (Fig. 548*A*); and when the patient is asked to tap, the tapping rate is usually similar to that of the tremor (Fig. 548*B*); tapping

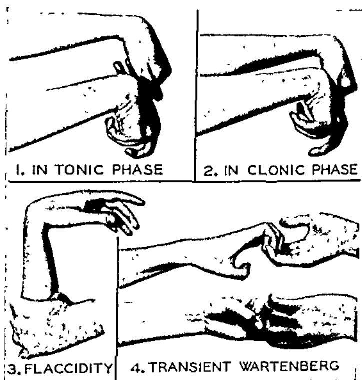


Fig 549. (Patient No. 15) Electrically induced convulsion, and post-convulsive phenomena (Courtesy of Dr. R. S. Lyman)

definitely never gets ahead of extrapyramidal tremor, nor does it stay significantly behind. The extrapyramidal tremor is usually abolished temporarily by hyoscine or modified by benzedrine or combinations thereof (Loman, Myerson, and Myerson). ***Hysterical tremor*** is usually faster

iest by the use of hypnosis; in this case the tremor was abolished during and after hypnosis (1941).

The study of the pattern of posture and movements during ***convulsive fits*** is important. In most fits of organic causation, abnormal reflexes can

i. e., the inability to stop a forceful active movement in order to avoid hitting an obstacle.

Figure 550 illustrates the proper technic of examination. Figure 551 shows the finger-to-nose test with eyes closed, recorded by a light attached to the index finger, in the upper picture performed by a normal person, in the lower picture performed by a patient suffering from multiple sclerosis … lous incoordination, brady- … the left arm and hand, pre- … ote in the case of the patient the wavy irregularities throughout the entire motion as well as the tremulous incoordination and slowing prior to reaching the goal. Figure 552 shows the same normal control and the same patient performing the finger-

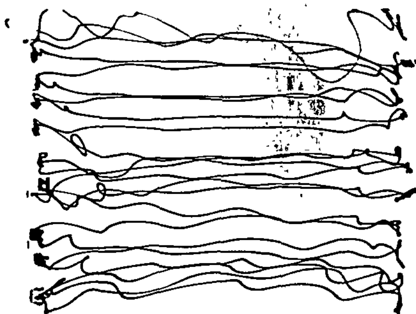


Fig 554. Photographic tracing of arm movements recorded by a light attached to the index finger, in a case of multiple sclerosis with left-sided cerebellar symptoms (patient No. 17). (Courtesy of Dr. R. S Lyman)

to-object-to-nose test with eyes open, and Fig 553 the finger-to-finger test with eyes closed Figure 554 shows the graphic record produced by the same patient, by passing his arm, with a light bulb attached to his index finger, between corresponding marked points along the sides of a frame from one side to the other, before an exposed photographic plate in an otherwise dark room.

The three-dimensional aspects of this incoordination (ataxia, dysmetria, bradyteleokinesis and intentional tremulous incoordination), however, are not adequately revealed by these two-dimensional recordings, but much better by Fig. 555, which was obtained by time exposure throughout the entire movement, with superimposed speedothron flashes in the end positions. The upper half of this figure (555) shows again the same normal

Coordination and Synergisms

The disturbances of the above named functions are known under the following names: (1) ataxia; (2) dysmetria (*overshooting*); (3) *adiadokokinesis*, i. e., inability to speedily perform alternating antagonistic



Fig 552. Finger-to-object-to-nose test, with eyes open. Upper: Normal individual. Lower A case of multiple sclerosis *with left-sided cerebellar symptoms (patient No. 17)* (Courtesy of Dr. R S. Lyman.)

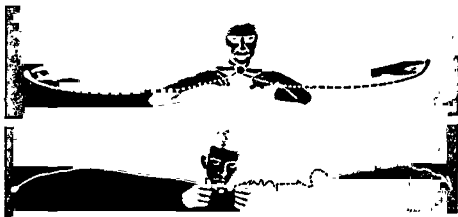


Fig 553. Finger-to-finger test with eyes closed. Upper. Normal individual. Lower: A case of multiple sclerosis with left-sided cerebellar symptoms (patient No 17) (Courtesy of Dr. R S Lyman)

movements; (4) "intentional tremor," better described as intentional tremulous incoordination, i. e., tremulous incoordination prior to reaching the goal of the movement; (5) bradyteleokinesis, i. e., slowing or stopping prior to reaching goal; (6) asynergia, usually expressing itself in irregular *stops, accelerations, and deflections;* and (7) the rebound phenomenon,

control, the lower half the same patient with left-sided cerebellar disturbance in multiple sclerosis. In Fig. 556 two revealing speedothron flash records of the same patient are mounted together, the one on the left illustrating the patient's normal right hand grabbing a glass of water, the one on the right illustrating the patient's disabled left hand trying to perform the same task, showing specifically the dysmetric disturbance of the grabbing movement, with its overshooting of spread of fingers, and over-

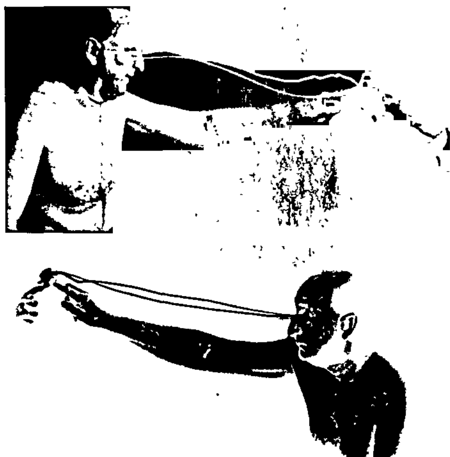


Fig 557. Left-sided hemiparesis with asynergic-athetoid disturbance, presumably due to right frontostriatocallosal lesion resulting from occlusion of right anterior cerebral artery (patient No. 3) Time exposure with light bulb tied to index finger, with speedothron flash at beginning of motion (Courtesy of Dr R S Lyman)

shooting toward the glass, the latter causing the water to spill before the glass is lifted off the table

Figure 557 shows the performance of the finger-to-object-to-face test performed by a patient suffering from athetoid and asynergic disturbance of the left hand and arm, presumably due to infarction resulting from occlusion of the right anterior cerebral artery. Note the irregular stops, accelerations and deflections when this patient performs the test with the left hand

The ability of the patient to stand with the eyes closed, feet close to-

Fig. 555 Photographic movement records with superimposed speedothron flashes in end positions Upper. Normal individual. Lower. Case of multiple sclerosis with left-sided cerebellar symptoms (patient No. 17) (Courtesy of Dr. R. S Lyman)



Fig. 556 Speedothron flash picture of normal right hand and disabled left hand grabbing a glass of water in a case of multiple sclerosis with left-sided cerebellar symptoms (patient No. 17) (Courtesy of Dr. R. S. Lyman)

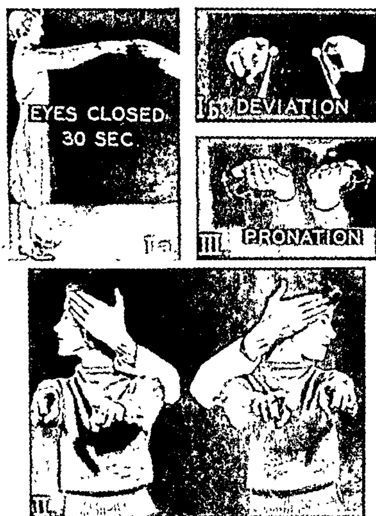


Fig. 559 Schilder and Hoff's postural reactions Normal individual (Courtesy of Dr R. S. Lyman)

gether and arms close to the sides of the body should always be investigated (Romberg's sign). It is positive when the ascending afferent spinal tracts are impaired.

Reflexes and Other More Complex Reactions, Including Postural Reactions

In briefly reviewing the reflexes it may be well to begin cranially and axially and progress caudally and peripherally.

Sucking Reflex. This is positive in cases of severe disturbance of consciousness. In the absence of disturbance of consciousness it may have more definite localizing value; it is frequently positive in cases of fronto-

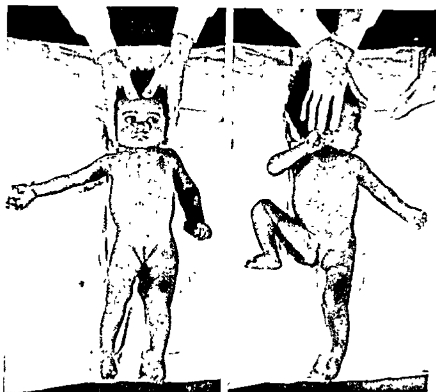


Fig. 558. Magnus and DeKleijn neck reflex. Child with decerebration on diencephalic level in tuberculous meningo-encephalitis (patient No 18) (Courtesy of Dr. R. S Lyman.)

striatal disturbance, e g., in cases of cerebral softening following occlusion of the anterior cerebral artery.

Magnus-DeKleijn Neck Reflex. When this *reflex is positive,* the arm toward which the jaw is turned becomes extended; the other arm flexed (extension of "jaw-arm," flexion of "occiput-arm," Fig. 558). Frequently the leg on the jaw side goes likewise into extension, the leg on the occiput side into *flexion, such as was the case in the patient shown in* Fig. 558. This neck reflex, when positive in a human being, denotes decerebration *on the thalamicodiencephalic level,* while in animals decerebration on the mesencephalic level (postrubral) is necessary in order to release this phenomenon.

is repeated with the arm outstretched above the horizontal plane. A slight amount of overshooting and undershooting is normal, corresponding to the appearance of fatigue in the lead arm and corresponding proprioceptive error. This error is exaggerated under certain pathological conditions, but has yet to prove its consistency as a reliable test. Normal subjects perform the first of these tests (that concerning spontaneous deviation) with rather variable accuracy, showing a considerable degree of spontaneous deviation (Fig. 560).



Fig. 561. Reactive abduction of arm when stepping sideways away from wall after leaning against it Normal individual (Courtesy of Dr. R S Lyman.)

A Simple Postural Reaction of Trunk and Arms. If a normal subject has been leaning with one arm and shoulder sideways against a wall and is then asked to step away from the wall, the arm which had been leaning against the wall exhibits abduction of considerable amplitude (Fig. 561).

Reflexes and Reactions of Arms and Hands. Of the tendon reflexes of the arms, the triceps reflex, the biceps reflex and the radius periosteal reflex should always be tested. They are absent or diminished in destruc-

Schilder and Hoff's Postural Reflexes and Reactions. These postural reflexes and reactions were developed in the wake of Magnus and DeKleijn's discoveries and although their clinical consistency has not yet been proven they should be studied as a matter of interest and potential further development; therefore, they are included in this review. There are four of them and they are pictorially illustrated in Fig. 559. The *first test* is that concerning spontaneous deviation of the outstretched arms and hands with eyes closed (Fig. 559, *Ia* and *Ib*).

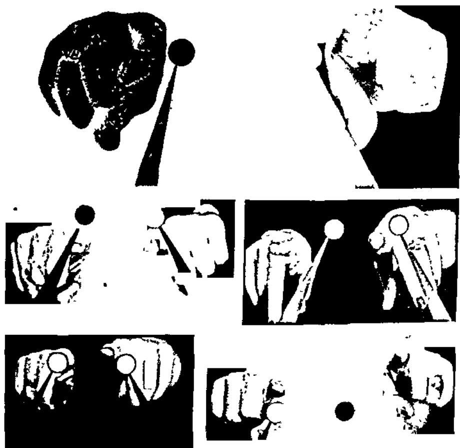


Fig. 560 Spontaneous deviations of outstretched arms, recorded by the position of the outstretched index fingers in relation to fixed markers Normal individuals (Courtesy of Dr. R. S. Lyman)

The *second test* concerns the question of elicitation of deviation of the outstretched arms and hands by passive turning of the head (Fig. 559, *II*).

tests.

The *fourth test* has to do with proprioceptive and body image factors. Its performance is illustrated and annotated in Fig. 559, *IV*. One arm is held outstretched below the horizontal plane for thirty seconds and the subject is then asked to raise the other arm to the same level; the same test

nore subtle sign than forced grasping. It is occasionally present in patients vith disturbance of consciousness; in the absence of disturbance of consciousness it is frequently present in hemipareses with striatal or thalamic in-



Fig. 563. Forced grasping, in a case of tumor (lipoma) of anterior and middle part of corpus callosum (patient No 19) (Courtesy of Dr R. S. Lyman)



Fig. 564. "Hooking" (Kleist's sign), in a case of tumor (lipoma) of anterior and middle part of corpus callosum (patient No 19) (Courtesy of Dr. R. S. Lyman)

volvement, in frontostriatal or frontothalamic involvement without paresis, often in psychotic states without organic neurologic disease, for instance, in certain cases of catatonic schizophrenia. This sign is related

tion or disturbance of the lower motor neuron, exaggerated in disturbance or destruction of the upper motor neuron. A peculiar slowing of the course of the tendon reflexes (delayed relaxation) occurs in myxedema.

The following five reflexes are useful in the diagnosis of diseases of the upper motor or corticospinal neuron:

Léri's Reflex This consists in a contraction of the biceps elicited by forceful passive flexion of the wrist joint and is therefore probably a noceoceptive reflex. This reflex is positive in normal persons, negative, i. e, absent, in cases of disturbance or destruction of the upper motor neuron.

Mayer's Reflex. Mayer's reflex is a similar noceoceptive reflex and consists in adduction and extension of the thumb upon forceful passive flexion of the ground phalanx of one or more of the other fingers, preferably the third or the fourth. It is likewise present in normal human beings and absent in interference or destruction of the upper motor neuron.

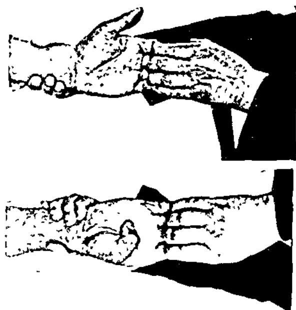


Fig. 562 Wartenberg's reflex. Above, normal side. Below, affected side. (From Wartenberg)

Trömner's Reflex, Wartenberg's Reflex, and Hoffmann's Sign. These are absent in normal individuals and positive in cases with disturbance or destruction of the upper motor neuron (Fig. 562).

Of the more complex reactions of the hand two should be specifically mentioned: (1) forced grasping (Fig. 563), which is related to frontothalamic mechanisms; it is absent in normal persons, but present in frontal as well as certain thalamic lesions; (2) "hooking" (Kleist). This sign is present and positive when the fingers of the hand of the patient, if gently elevated by the fingers of the examiner, will hook into the fingers of the examiner as shown in Fig. 564. In this figure the hand shown at the left is that of the patient, the hand shown at the upper right is the hand of the examiner. This sign is negative in normal human beings. It is invariably positive in patients who show forced grasping, but it is frequently present in patients who do not show forced grasping and is therefore a

ionally be suppressed in states of emotional tension, e. g., hysterical disurbances. The upper, middle, and lower abdominal reflexes for each side hould always be examined and recorded separately. Proper examinaion of the abdominal reflexes should always include their repetition at noderately frequent intervals in order to test their exhaustibility In ases of multiple sclerosis the abdominal reflexes may seem perfect at he first try but may disappear because of exhaustibility after two or more rials.

Reflexes of the Legs. Like all tendon reflexes the knee jerk and the nkle jerk are absent or diminished in lesions of the lower motor neuron, xaggerated in lesions of the upper motor neuron. The question of presnce of patellar clonus or ankle clonus, which are frequently associated vith exaggeration of the knee and ankle reflexes, should always be investiated by the well-known maneuvers used for their elicitation.

Babinski's Plantar Reflex. This is the most important and clinically *he most consistent reflex. In view of its great clinical importance and* pecificity, particular care is indicated in the technic of its elicitation. If he skin at the outer border of the foot is rather lightly stroked with a noderately sharp point, normal persons will react with a slight plantar lexion of all toes. We then say that the sign of Babinski is negative In ases of disturbance or destruction of the pyramidal tract, however, the ame maneuver will call forth dorsiflexion of the big toe and fanning (spreadng) of the small toes, usually associated with a contraction of the tensor asciae latae at the thigh. This is the positive sign of Babinski.

This sign is extraordinarily reliable, however, if the proper technic is not followed and particularly if the most frequent mistake is committed, namely, too heavy stroking with subcutaneous pressure, the positive sign of Babinski may occasionally be obscured through interference by the grasp reaction which, although occasionally present in pyramidal lesions, is regularly present in frontal lesions, and particularly if there is a combination of frontal and pyramidal lesions One should never forget that the Babinski reflex is a pure skin reflex and subcutaneous pressure should never be used, especially because of the danger of obscuring a positive sign of Babinski by the grasp elicited by deep subcutaneous pressure. Figures 565*A–D* *illustrate this point rather strikingly. These photographs were* taken from the foot of a female patient who was suffering from an extensive bilateral frontocentral degenerative process, either of the nature of vascular infarction or of extensive presenile atrophy. The disturbance was bilaterally identical and the condition of the right foot in this case, which is shown in Figs 565*A–D*, is representative also of that of the left foot. At rest there was slight permanent equinovarus position of either foot with permanent slight dorsiflexion of the great toe (Fig 565*A*) Rather light stroking of the outer border of the foot with a moderately sharp point produced a typical positive sign of Babinski proving the presence of interference with the pyramidal tract (Fig 565*B*). Heavy pressure with the handle of the reflex hammer applied in the planta produced flexion of all toes with definite inner rotation of the foot, i. e , the so-called "grasp" (Fig. 565*C*). This could be either *a special aspect of the pyramidal disease or a* sign of associated frontal disturbance. Whenever an attempt was made in this case to elicit the sign of Babinski by heavy stroking such as is frequently done by inexperienced observers, neither a positive sign of Babin-

to the more subtle mechanisms of motor assent and motor negativism which occur in schizophreniform psychoses as well as in organic neurologic disease. Another still more subtle sign of motor assent is active accompaniment of passive movements.

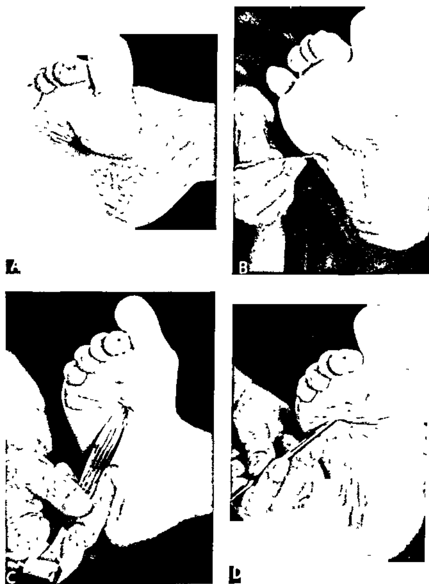


Fig 565. *A, B, C, D:* The sign of Babinski (*B*), the "grasp" (*C*) and their mutual interference (*D*), illustrated in the case of a woman with bilateral pyramidal and frontal involvement (patient No 20). (Courtesy of Dr. R. S. Lyman)

Abdominal Reflexes. The abdominal reflexes are present in normal human beings, absent or diminished in cases of destruction or disturbance of the upper motor neuron, i. e., the pyramidal tract. It is well to remember, however, that the abdominal reflexes, like all skin reflexes, may occa-



Fig. 567. The rising synkinesia *A*, In a normal individual *B*, In a patient suffering from spastic paraparesis of both legs, due to bilateral pyramidal lesion presumably of the motor leg area caused by a gun-shot wound at the vertex (patient No 21) (Courtesy of Dr R. S. Lyman)



Fig. 568 The rising synkinesia in a patient suffering from a right frontostriatocallosal lesion, presumably due to occlusion of right anterior cerebral artery (patient No. 3). (Courtesy of Dr. R. S. Lyman)

ski nor a typical grasp resulted, but instead nonspecific flexion of the small toes and slight inner rotation of the foot appeared in this case (Fig. 565*D*) as well as in many others if examined in this faulty way.

Sometimes Babinski's maneuver, correctly carried out, may produce no reaction of the toes whatsoever. We then speak of a "mute planta." Although this absent reaction may occasionally denote a subtle interference with the integrity of the pyramidal system, it must be realized that more frequently such absence of reaction to a skin reflex may be due to emotional tension or rather due to conversion-dissociation of a psychologic nature, such as is present in hysterical states.

Other toe reflexes denoting lesions of the pyramidal tract are the following:

Oppenheim's Sign. Stroking down along the medial margin of the shin with pressure upon the periosteum produces dorsiflexion of the big toe in cases of pyramidal disease.

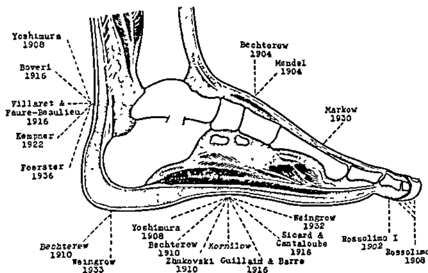


Fig 566 The accessory toe reflexes and their unified interpretation as elicited by stretching of the plantar musculature (From Wartenberg)

Gordon's Sign. Strong pressure (squeezing) of the calves produces dorsiflexion of the big toe in cases of lesions of the pyramidal system. Both Oppenheim's and Gordon's signs are probably noceoceptive.

Mendel-Bechterew Sign. Hitting the region of the cuboid bone with a reflex hammer produces quick plantar flexion of the small toes in cases of lesions of the pyramidal system

Rossolimo's Sign. Hitting the ball of the foot at the points of articulation of the metatarsal bones with the ground phalanges of the toes with a reflex hammer, or a quick lifting snap applied to the tips of the small toes with the examiner's fingers, produces quick plantar flexion of the small toes in cases of lesions of the pyramidal system, while in normal individuals either no reaction or a quick dorsiflexion of the small toes takes place. Wartenberg has pointed out that both Rossolimo's and Mendel-Bechterew



Fig. 570. The bending over synkinesia (Néri's sign) *A*, In a normal individual. *B*, In a patient suffering from spastic paraparesis of the legs, presumably due to bilateral injury of the motor leg area caused by a gun-shot wound at the vertex (patient No. 21) (Courtesy of Dr. R. S. Lyman.)



Fig. 571. The bending over synkinesia (Néri's sign) showing flexion of the paretic left leg in a patient suffering from a right frontal lesion (patient No. 22) (Courtesy of Dr R. S Lyman)

over his chest the thigh will remain motionless and the heels will be pressed down against the examining table (Fig. 567*A*). In case of lesion of the

Synkinesias

The examination of the synkinesias is that part of the neurologic examination which requires the greatest skill and refinement. They are admirably presented in Lévy-Valensi's and in Kroll's textbooks as well as by Foerster in Bumke and Foerster's handbook, although Foerster's presentation, in view of its abundance of material, is somewhat confusing to the student. The best and most clear-cut presentation is definitely that by Lévy-Valensi. However, even Lévy-Valensi does not always satisfy the student in regard to clinical specificity and consistency of these signs. In

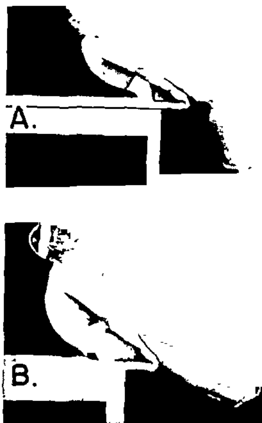


Fig. 569. The leaning backward synkinesia. *A*, In a normal individual. *B*, In a patient with gun-shot wound at the vertex, which presumably caused bilateral lesion of the motor leg area (patient No. 21). (Courtesy of Dr. R. S. Lyman.)

the following we shall review the synkinesias on the hand of Lyman's pictorial material which has been accumulated with special attention to the question of consistency and clinical specificity of these signs. In the following I shall group the synkinesias into three groups: (1) those elicited by active trunk movements; (2) those elicited by active and passive movements of arms or hands; and (3) those elicited by active and passive movements of the legs.

Synkinesias Elicited by Active Trunk Movements. *Flexion of Thigh Associated with Flexion of Trunk (Babinski).* In the normal individual sitting up from the recumbent position with his arms crossed



Fig. 570. The bending over synkinesia (Néri's sign) *A*, In a normal individual *B*, In a patient suffering from spastic paraparesis of the legs, presumably due to bilateral injury of the motor leg area caused by a gun-shot wound at the vertex (patient No 21) (Courtesy of Dr. R. S. Lyman.)



Fig. 571. The bending over synkinesia (Néri's sign) showing flexion of the paretic left leg in a patient suffering from a right frontal lesion (patient No. 22). (Courtesy of Dr R. S. Lyman.)

over his chest the thigh will remain motionless and the heels will be pressed down against the examining table (Fig. 567*A*). In case of lesion of the

pyramidal tract, however, flexion of the trunk under these circumstances is associated with flexion of the thigh in the hip joint, causing the leg, flexed in the thigh, to be raised up, the heel being elevated off the examin-

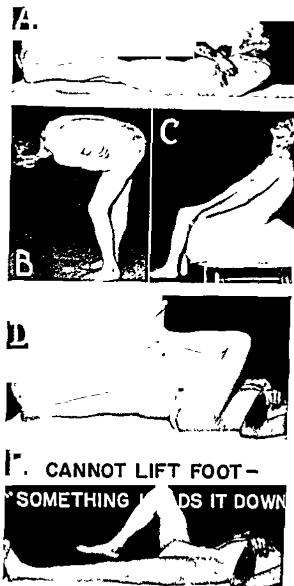


Fig. 572. Synkinesias associated with active trunk and leg movements in a patient suffering from right sided hysterical hemiparesis *A*, The rising synkinesia *B*, The bending over synkinesia *C*, The bending backwards synkinesia. *D*, The synkinesia of the foot associated with active voluntary hip and knee flexion on the left *E*, The synkinesia of the foot associated with active voluntary hip and knee flexion on the right (patient No. 23). (Courtesy of Dr R S. Lyman)

ing table (Fig
of both legs d
at the vertex.
gia, occasionally with the addition of slight flexion of the knee and plantar

flexion of the foot (climbing synergia). This is shown in Fig. 568 in a case of left-sided frontostriatal asynergia, presumably due to occlusion of the right anterior cerebral artery, probably with callosal involvement which may account for the slight hip and knee flexion recognizable in the right

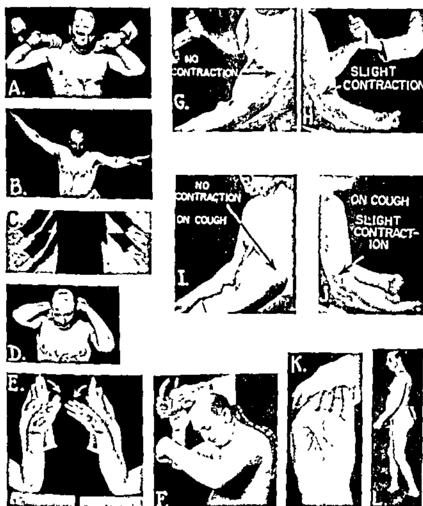


Fig 573 The synkinesias of arms and hands in a patient with organic left-sided hemiparesis with asynergia and athetoid phenomena, presumably due to right-sided frontostriatocallosal lesion caused by occlusion of the right anterior cerebral artery (patient No 3). *A*, Babinski's tonus test *B*, Souques' test *C*, Babinski's pronation sign *D*, Strumpell's pronation sign *E*, Raimistes' hand test. *F*, Bechterew's arm sign *G* and *H*, The test of triceps contraction on contralateral forceful biceps innervation *I* and *J*, The arm muscle reaction to coughing *K*, The Klippel-Weil test. *L*, The arm in walking (Courtesy of Dr R. S Lyman)

leg also. In hysterical paresis, however, the heels remain on the examining table (Fig 572*A*).

Triple Extension of Leg Associated with Extension of Trunk A normal individual sitting on the edge of an examining table holding on with his hands to the edge of the table, if asked to lean over backward as far

as his arms will stretch, while his legs hang down without support at the feet, will be able to do so without changing the position of his dangling legs significantly (Fig. 569*A*). In pyramidal paraparesis, however, illustrated in the case of the same patient with gun-shot wound at the vertex, who was shown in Fig. 567*B*, the legs will go into triple extension (Fig. 569*B*). In hysterical paresis, however, the legs will remain dangling as in the normal patient (Fig. 572*C*).

Knee Flexion Associated with Flexion of the Trunk in Standing Position (Néri). This occurs in lesions of the upper motor neuron, illustrated in Fig. 570*B*, again in the patient with the gun-shot wound at the vertex. In a normal individual the knees will remain extended (Fig. 570*A*). Fig. 571 shows Néri's sign to be positive on the paretic-asynergic left side in a patient presumed to suffer from the sequelae of a right frontal lesion. In the case of right hysterical hemiparesis, shown in Fig. 572, the right "paretic" leg remains extended while the patient bends the left normal leg and bends demonstratively over toward the left side (Fig. 572*B*).

Synkinesias Elicited by Active and Passive Movements of Arms or Hands. *The Phenomenon of Exaggerated or Reduced Flexibility of the Forearm (Babinski).* This sign is not actually a synkinesia in the strict sense of the word, but merely a phenomenon indicative of the state of tonus. However, it is usually listed with the synkinesias in view of the importance which tonus has in relation to them. This sign is performed by passive flexion of the forearm against the upper arm, while the upper arm is elevated in the shoulder (Figs. 573*A*, 574*A*, and 575*A*). This sign is by no means specific but allows a fairly good photographic record of the state of tonus In the patient shown in Fig. 573 and who is suffering from an organic lesion, the asynergic and slightly hypertonic-paretic left arm cannot be bent to quite as acute an angle as the right arm (Fig. 573*A*). However, in organic as well as in psychogenic states of reduction of tonus exaggerated flexibility may be present such as shown in Fig. 574*A* in the "paretic" left arm of a malingerer and in Fig. 575*A* in the "paretic" right arm of a patient suffering from right hysterical hemiparesis.

The Interossei Phenomenon (Souques). If a patient with an organic paresis arising from disturbance of the frontal or pyramidal system carries out the request to elevate his extended arms, the fingers of the paretic hand will show overextension and spread (Fig. 573*B*).* In malingering or hysterical weakness, however, the fingers will show neither overextension nor spread (Figs. 574*B* and 575*C*).

Babinski's Pronation Phenomenon. If the arms are passively abducted with the hands in supination and then suddenly released, the organic hemiplegic or hemiparetic arm usually shows pronation of the hand when falling back toward the body, while the normal or psychogenically paralyzed extremity will fall back toward the body in supinated position. Although this sign is undeniable and striking when clearly positive, a suggestive positive reaction cannot be taken at face value, but will have to be interpreted in the light of general conditions of tonus of the arm as a whole. Furthermore, if the sign is negative or only suggestively positive, it does not exclude organic involvement of the frontal or pyramidal system. As seen in Fig. 573*C*, it was found to be only slightly positive in the left paretic-asynergic extremity of a patient suffering from an organic frontostria-

* The bilateral response in this case is probably due to the callosal involvement.

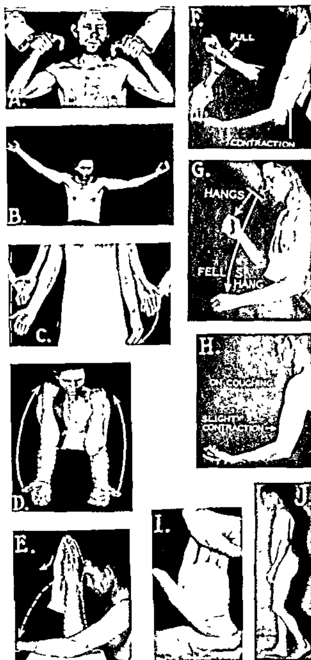


FIG. 574. The synkinesias of arms and hands in malingered left-sided "hemiparesis" (patient No 8) *A*, Babinski's tonus test *B*, Souques' test. *C*, Babinski's pronation sign *D*, Strumpell's pronation sign *E*, Raimistes' hand test *F*, The test of triceps contraction on contralateral forceful biceps innervation *G*, Bechterew's arm sign *H*, The arm muscle reaction to coughing. *I*, The Klippel-Weil test *J*, The arm in walking. (Courtesy of Dr. R. S. Lyman)

tocallosal lesion, while it was more than suggestively positive although not completely positive in the case with malingered left hemiparesis (Fig.

574*C*). However, it was negative in the case of hysterical hemiparesis (Fig. 575*B*).

The Pronation Phenomenon of Strümpell. The patient is asked to bring his hand to his shoulder by flexion of the elbow. The normal individual will bring the palm of the hand to the shoulder with the hand in supination. *In organic hemiparesis,* this movement will be accompanied by

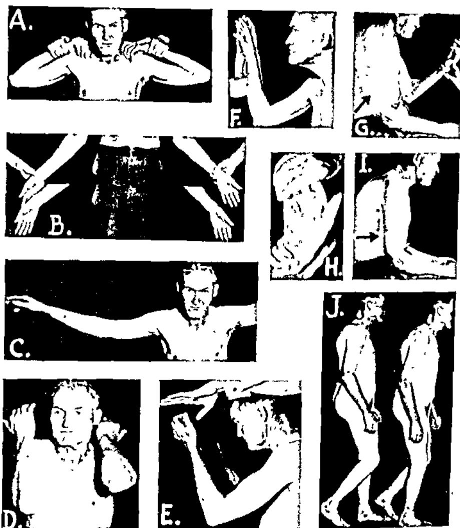


Fig 575. The synkinesias of arms and hands in right-sided hysterical hemiparesis (patient No. 23) *A*, Babinski's tonus test *B*, Babinski's pronation sign. *C*, Souques' test *D*, Strumpell's pronation sign. *E*, Bechterew's arm sign. *F*, Raimistes' hand test *G*, The test of triceps contraction on contralateral forceful biceps innervation. *H*, The Klippel-Weil test. *I*, The arm muscle reaction to coughing. *J*, The swinging movements of the arms in walking. (Courtesy of Dr R. S. Lyman.)

pronation so that the dorsum of the hand will approach the shoulder, the palm looking forward. This phenomenon was not positive in the case of right frontostriatal involvement, although the movements show a certain amount of apraxic clumsiness (Fig. 573*D*). It was negative in the malingerer as well as in the case of hysterical hemiparesis (Figs. 574*D* and 575*D*).

Raimistes' Arm Sign. The elbow of the patient is placed on a table,

forearm and hand in vertical position, the hand of the patient being maintained in that position by the examiner's hand being placed against it. If the examiner's hand is suddenly removed, the patient's hand, if paralyzed or paretic due to pyramidal involvement, will drop to form an angle of 130–140 degrees with the forearm; while the normal, the frontal-asynergic or hysterically paralyzed hand will drop only slightly or not at all (Fig 573E and Fig. 575F). *The malingerer shown in Fig. 574E lets his whole* arm drop dramatically on this occasion.

Bechterew's Sign. If both arms, flexed at the elbow, are passively elevated in the shoulder and then suddenly released, normal or hysterically paralyzed patients will not drop the arm immediately but for a moment or longer the arm will hang in midair (Fig. 575E). This "hang" may be



Fig. 576. The synkinesia of the foot associated with active voluntary flexion of hip and knee joints. *A*, In a normal individual *B*, In a patient with injury of the motor leg area due to gun-shot wound at the vertex (patient No 21) (Courtesy of Dr. R S Lyman)

exaggerated in cases of organic hemiplegia or hemiparesis even if not associated with an appreciable increase in tonus. It is well to note that the reaction in this respect was normal in the case of frontal involvement (Fig. 573F). The malingerer, however, let his left "paretic" arm drop without a "hang" (Fig. 574G).

Associated Contralateral Contraction of the Triceps on Flexion of the Other Arm by Biceps Action This contraction is present in normal individuals, in hysterically hemiparetic patients (Fig. 575G) and in malingered hemiparesis (Fig. 574F). In organic hemiparesis, it is present in the normal arm when the paretic arm performs the forceful biceps flexion (Fig. 573H); however, it may be absent in the paretic arm when the normal arm performs the forceful biceps flexion (Fig. 573G).

Triceps or Biceps Contraction Associated with Coughing. This is present in the normal arm (Fig. 573*J*). In organic hemiparesis it may be absent in the paretic arm (Fig. 573*I*) or it may be exaggerated. It is present in hysterical and malingered hemiparesis (Figs. 574*H* and 575*I*).

Flexion of the Thumb Associated with Passive Extension of the Other Fingers (Klippel-Weil). This sign is positive in organic hemiparesis (Fig. 573*K*), negative in normal individuals, in malingered hemiparesis (Fig. 574*I*) and in hysterical hemiparesis (Fig. 575*H*).



Fig. 577. The synkinesias of the foot associated with active voluntary flexion of the hip and knee joints in a patient with right-sided frontostriatocallosal lesion (patient No. 3). (Courtesy of Dr. R S Lyman.)

Symmetric Associated Movements of One Arm Produced by Active Movements, Passive Movements or Electrical Stimulation of the Other. Such associated movements occur in a variety of organic cerebral diseases with cortical, subcortical and brain stem involvement (e. g., *infantile* hemiplegias, encephalitides), occasionally as a rare curiosity in otherwise normal human beings. They have been described in detail by Alexander (1932), who also reviewed the older literature. They may be elicitable in the paretic or paralyzed extremity from the normal extremity and vice versa.

Synkinesias Elicited by Active and Passive Movements of the Legs. *The Associated Swinging Movements of the Arms While Walking.* The normal swinging movements of the arms while walking are absent in parkinsonism, presumably due to the nigral or pallidal involvement, in unilateral cases on the side opposite to the cerebral lesion. It should be emphasized that this loss is frequently a subtle and early sign of beginning postencephalitic degeneration or other extrapyramidal disease, but one should keep in mind that bilateral absence of associated movements in walking may occur in certain catatonic psychotic states, even when they are not symptomatic manifestations of a postencephalitic process, such as occasionally they are (Alexander, 1941). Furthermore, these associated movements are absent or reduced in the organic hemiparetic or hemiparalyzed

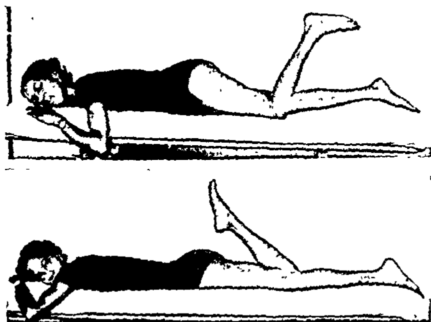


Fig 578. (Patient No. 22.) Upper. Triple flexion (flexion of hip and foot) associated with active voluntary flexion of the left knee, in the paretic left leg of a patient suffering from a right frontal lesion Lower. Extension of foot without hip movement in active voluntary flexion of the knee of the right normal leg of the same patient. (Courtesy of Dr R. S. Lyman.)

arm; in such cases the arm is usually held in flexion (Fig. 573*L*). In hysterical and in malingered hemiparesis or hemiparalysis the arm usually shows normal associated swinging movements (Fig. 575*J*), but in a number of such cases the arm may hang down limply (Fig. 574*J*), such as it does, of course, in peripheral nerve paralysis.

Triple Flexion and "Climbing" Synergia. If a normal individual is asked to flex hip and knee joints, his foot will show extension (plantar flexion, Fig. 576*A*), while a pyramidally hemiparetic limb will show flexion (dorsiflexion) of the foot (Fig. 576*B*). We call this phenomenon triple flexion because flexion (dorsiflexion) of the foot becomes associated with flexion of knee and hip, whereas normally it is not. In certain frontal lesions, extreme plantar flexion with inner rotation (supination) of the

foot may become associated with hip and knee flexion (climbing synergia) (Fig. 577, upper).

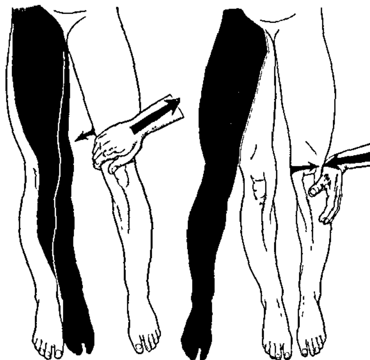


Fig 579. Raimistes' leg sign Abnormal leg in black, normal in white. If the examiner opposes active adduction of the normal leg, the abnormal leg performs adduction; if the examiner opposes abduction of the normal leg, the abnormal leg performs abduction (From Lévy-Valensi)

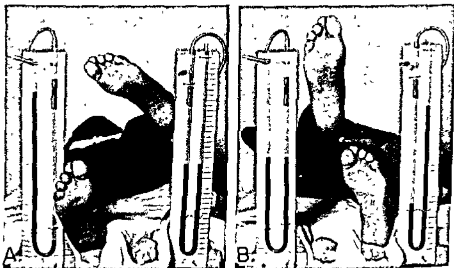


Fig 580. The Hoover test in organic left hemiparesis presumably due to right frontal lesion (patient No 22). (*Courtesy of Dr R. S. Lyman*)

Active knee flexion in prone position is normally associated with extension (plantar flexion) of the foot (Fig. 578, lower). In frontal or pyramidal involvement triple flexion takes place, i. e., active flexion of the knee in

prone position becomes associated with flexion (dorsiflexion) of the foot and with flexion (elevation) of the hip (Fig 578, upper).



Fig 581. The Hoover test in hysterical right "hemiplegia" (patient No 24) (Courtesy of Dr R S Lyman)

Raimistes' Leg Sign If the examiner opposes adduction or abduction of the thigh and leg on the normal side, the pyramidally paralyzed or paretic leg will carry out a movement identical with that which was forcefully prevented in the other normal leg (Fig. 579) Raimistes' leg test,

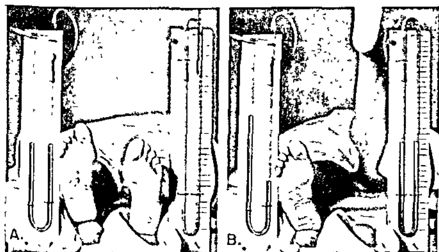


Fig. 582. The Hoover test after slight improvement following the first session of hypnotic psychotherapy, in the same patient with right hysterical "hemiplegia," shown in Fig. 581. (Courtesy of Dr R. S Lyman)

therefore, is a useful maneuver to bring out a latent tendency to symmetric homologous associated movements, which follow the same general rules as those of the arms

Hoover Test (Phenomenon of Complementary Opposition, Grasset and

Gaussel). If a normal individual in recumbent position raises one leg up high, the other will press down on the examining table. This pressing down movement can be recorded quantitatively by a manometer, with a rubber bulb placed under the heel. When a patient suffering from an organic hemiparalysis or weakness lifts the paretic leg or attempts to lift

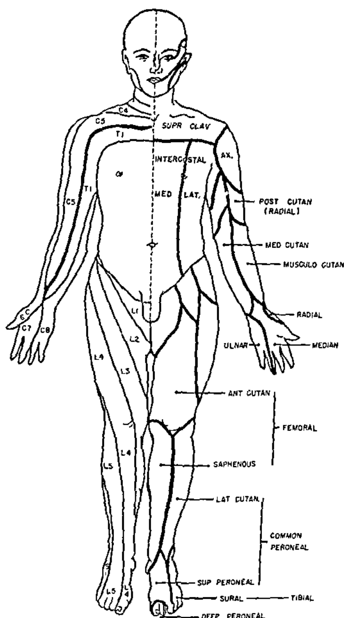


Fig. 583. Chart for sensory examination (*After Keegan; courtesy of Dr Arthur A Ward, Jr.*)

the paralyzed leg, the other leg will press down with great force; however, when he lifts the normal leg, the pressing down movement of the paralyzed or paretic leg will be absent or reduced respectively. The opposite is the case in hysterical or malingered paralysis or weakness. When lifting the normal leg, the hysterically paralyzed leg will press down like a normal

leg; however, when attempting to lift or when slightly lifting the hysterically or fallaciously "paralyzed" or "paretic" leg, the down-pressing movement of the normal leg will be absent or trifling, commensurate to the absence or paucity of effort made. Fig. 580 shows the Hoover test in a patient suffering from an organic, presumably frontal, lesion. When lifting

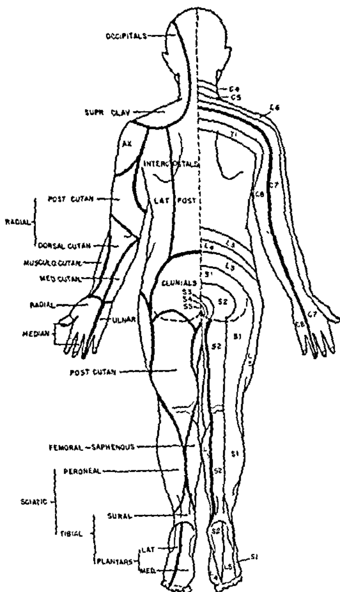


Fig. 584. Chart for sensory examination (After Keegan; courtesy of Dr. Arthur A Ward, Jr)

the paretic left leg with a certain amount of circumduction (Fig. 580*A*), the normal right leg carries out good complementary downward pressure, as recognizable by the rise in the corresponding manometer. When elevating the normal right leg, the paretic left leg performs a somewhat less strong complementary downward pressure (Fig. 580*B*).

Figure 581 shows a patient suffering from right hysterical hemiparalysis. When attempting to lift the right "paralyzed" leg, the left normal leg performs only trifling downward pressure (Fig. 581*A*). However, when raising the left normal leg, the right "paralyzed" leg presses down so hard that the mercury can be seen squirting out of the top of the manometer in this speedothron flash picture (Fig. 581*B*). Figure 582 shows the same patient after one treatment by hypnotic psychotherapy. The patient now can lift the right leg slightly and there is a good compensating downward pressure of the left leg, indicating effort (Fig. 582*A*): the mercury in the manometer associated with the left foot squirts out at the top.

Gait One of the most important synkinetic performances is the gait. It should always be studied and described in detail; for purposes of record a detailed and complete description in as simple terms as possible is far preferable to a one-label diagnosis. Scientific standards of study may be attained by the use of the methods developed by Plato Schwartz and his coworkers. The study of Morton's book may prove useful in understanding gait and its problems.

THE SENSORY EXAMINATION

The sensory examination should include: (1) all qualities of sensation of the skin: fine touch examined with a brush or wisp of cotton, pain examined with a pin, temperature examined with hot and cold glass tubes. Quantitative data may be obtained by the use of two-point discrimination and of a set of graded "von Frey hairs." (2) Position sense of arms, hands, fingers, legs, feet, and toes (3) Vibration sense over the bony prominences; and (4) stereognosis (ability to recognize objects by touch and grasp with eyes closed). This may be combined with a test for recognition of surface texture and materials.

A chart for the recording of sensory modalities is depicted in Figs. 583 and 584.

COMA

Coma may be defined as a state of unconsciousness so deep that the patient cannot be aroused by even the most powerful stimuli The examination of the comatose patient demands inquiry into the circumstances preceding the state of coma, a complete physical examination and, frequently, laboratory studies of the spinal fluid, blood and urine. For the differential diagnosis of the various causes of coma, the reader is referred to Dr. Gray's chapter in the first edition of this book as well as a recent, excellent paper by Mount

THE EXAMINATION OF THE SPINAL FLUID

The examination of the spinal fluid is of extraordinary importance. The most significant data concerning it would fill an entire chapter; instead of including a discussion insufficient because of brevity, the student is referred to Merritt and Fremont-Smith's excellent book. The following basic data should always be obtained in connection with a lumbar puncture.

1. The spinal fluid pressure should be recorded with a graded glass tube in terms of millimeters of water, with the patient recumbent on his side.

2. "Spinal fluid dynamics" refers to the pressure response elicitable by jugular and by abdominal compression. The most frequent mistake made in the examination of the spinal fluid dynamics is inadequate atten-

tion to the speed of rise and fall. Slow rise and slow fall on jugular compression with rapid rise and fall on abdominal compression is definitely indicative of partial block.

3. After examination of the dynamics, the number of cc. removed should be annotated and the final pressure recorded, in order to be able to compute the Ayala index.

4. The type of cells contained in the spinal fluid should be determined and the number of cells per cubic millimeter should be counted.

5. Determination of the total protein content, if feasible also of the globulin fraction, per 100 cc. of spinal fluid should always be carried out. A preliminary impression as to the globulin content may be gained by the Pandy test.

6. The Wassermann reaction

7. The colloidal gold or mastic test.

X-RAY EXAMINATION OF THE NERVOUS SYSTEM

Stereo-x-rays of skull and spine should be performed as a matter of routine in neuropsychiatric cases. Special attention should be given particularly to the sella turcica, the clinoid processes, and the petrous bone. Certain cases require special studies by injection of air into the ventricular and subarachnoid system (pneumo-encephalography) either by the ventricular or the spinal route Lipiodol and other contrast media should be limited to the spinal system. Arteriography is indicated for the localization of aneurysms. The entire problem and the technics of x-ray examination of the nervous system are too complex to be dealt with within the framework of this chapter. The student is therefore referred to the recent excellent books by Davidoff and Dyke and by Pancoast, Pendergrass and Schaeffer Of great usefulness in the interpretation of the x ray findings in terms of cerebral localization is the compact series of craniocerebral schemata by A. Schuller (Urban and Schwarzenberg, Vienna, 1931).

BRAIN WAVES (ELECTROENCEPHALOGRAPHY)

Every well-equipped neuropsychiatric clinic should have facilities for examination of the brain waves, and private practitioners of neuropsychiatry should either be able to refer their patients to a brain wave laboratory or install such facilities in their own offices Their greatest usefulness is in the differential diagnosis of convulsive disorders and in the localization of brain tumors.

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XIX

THE ENDOCRINE SURVEY

In recent years, there has evolved a fundamental change in our concept of endocrinology—that of regarding the human body as a going concern with definite functions to perform rather than as a cosmetic structure resulting from the interrelationship and dependence of the various endocrine glands. Whereas the older school of descriptive endocrinologists evaluated the endocrine status of the patient by appraisal of the body habitus—anthropometric measurements and alterations in osseous growth and fat padding—the present school subscribes to the more tenable approach that diagnosis of various endocrinopathies is dependent upon the whole clinical picture, with especial reference to the functional capacity, rather than the more limited anatomic viewpoint As the orthopedist is interested primarily in the restoration of function in a fractured extremity rather than the cosmetic deformity, so is the endocrinologist of today content with a similar functional point of view, both in diagnosis and therapy. With that concept uppermost in mind, we shall proceed to the brief consideration of endocrine diagnosis

The term "endocrine survey" applies to the diagnostic procedures to be pursued in the endocrine evaluation of the individual patient. This considers the following methods of investigation: (1) the endocrine history; (2) physical examination; (3) roentgenologic investigation; and (4) special laboratory studies. In this chapter, we shall discuss chiefly the methods applicable to physical diagnosis but will indicate those instances wherein further study may be contributory to diagnosis.

THE ENDOCRINE HISTORY

A complete history is essential, not only for the evaluation of the endocrine complaint but also for the equally important reason that it recognizes systemic disease and psychiatric disabilities. Diverse endocrine alterations may result from chronic debilitating states, these indirect effects being mediated via the pituitary gland. A detailed medical history, therefore, lends considerable insight into the growth and development and interrelationships of the various body processes. Particularly, an exhaustive investigation of the family, developmental, marital and reproductive history is invaluable.

PHYSICAL EXAMINATION

Search for both constitutional and mental disorders should be instituted. In addition, the endocrine aspects of the physical examination consider certain objective data, e g., habitus, skin, distribution of hair, facies, and sexual development.

Habitus

This may be suggestive of several distinct endocrinopathies. The habitus is determined by general inspection of the patient as a whole.

Retarded Skeletal Growth (Dwarfism). Hamblen recognizes three types of dwarfism: simple dwarfism in which there is general statural retardation; dwarfism associated with genital hypoplasia; and dwarfism associated with genital overdevelopment.

Simple dwarfism may, in turn, be subdivided into two forms: true or proportionate dwarfism, and disproportionate dwarfism. The true dwarf is an individual who appears to be an adult in miniature; no statural or reproductive defects are demonstrable and no endocrine implications exist. This type of dwarfism is hereditary, being related to chromosomal constitution. Disproportionate dwarfism, on the other hand, is dependent on statural retardation resulting from primary affections of osseous development (achondroplasia, chondro-osteodystrophy, dyschondroplasia, osteogenesis imperfecta) or secondary disturbances in osseous growth (rickets, scurvy, tuberculosis, syphilis, etc.).

Dwarfism with genital hypoplasia refers to those instances wherein skeletal and sexual retardation persist in the adult period. Premature senility (progeria) may be associated. The etiologic factors may be endocrine or constitutional. Among the endocrine causes of this form of dwarfism may be included childhood hypothyroidism, juvenile and adolescent hypogonadism, hypo-antuitarism, adiposogenitalism and adrenogenitalism (female); these will be considered in more detail in the following chapter. The constitutional entities leading to dwarfism with genital hypoplasia include congenital constitutional inadequacy, congenital heart disease and valvular heart disease early in childhood, chronic debilitating states of diverse types, faulty nutrition arising from inadequate diet or gastroenterologic affections, renal rickets, and various psychopathies of childhood.

Dwarfism with genital overdevelopment results from excessive production of the sex steroids from such causes as granulosa cell ovarian tumor, testicular tumor, and adrenal cortical adenoma or hyperplasia. Precocious sexual development occurs which approaches adult proportions Premature epiphyseal closure is stimulated, leading ultimately to dwarfism in spite of early statural growth.

Accelerated Growth (Giantism). Statural overgrowth may be normal or dependent on the failure of epiphyseal closure If the epiphyses remain open as a result of hypogonadism, either of the testes or ovaries, the growth factor of the pituitary gland will promote overgrowth of the long bones This type of hypogonadal individual is characterized by excessive tallness, long extremities as compared with a relatively short trunk, hypoplastic genitalia and underdevelopment of the secondary sexual characteristics. The occurrence of eosinophil tumors of the pituitary gland prior to the period of normal epiphyseal closure, i e, around fourteen to sixteen years in the woman and sixteen to eighteen years in the male, results in pronounced statural overgrowth but normal or advanced genital development —giantism. Should hyperfunction of the anterior pituitary gland appear after epiphyseal closure has taken place, overgrowth of the acral bones results in the acromegaloid state. Hyperthyroidism during childhood leads to a sharp increase in growth rate but the epiphyses close at the normal time.

Obesity. Obesity is a state of being overweight. Obesity may be classified into three forms: exogenous, endocrine and localized.

Exogenous Obesity. Exogenous or alimentary obesity results from greater caloric intake than that necessary to meet the body demands. This is the commonest affliction of mankind The obesity is well distributed, symmetrical and rarely painful.

Endocrine Obesity. This refers to those types of localized depositions of fat in which the regional predilections are characteristic of the particular gland involved. This type of obesity is usually ascribable to hypofunction of the thyroid and gonads, to alterations in the hypothalamico-pituitary relationships (Frohlich's syndrome), and to peculiar hyperfunctioning states of the pituitary or adrenal cortex (basophilism) The hypothyroid form of obesity consists of mucinous infiltration of the subcutaneous tissues resulting in thickening and coarseness of the skin Hypogonadal obesity results in deposition of fat about the pelvic girdle and lower extremities. In the hypothalamico-pituitary form of obesity, a characteristic girdle-like deposition of fat occurs. A "buffalo" type of obesity occurs in basophilism, whether it be due to pituitary basophilism or adrenal cortical hyperplasia or tumors, the fat being distributed chiefly to the torso and neck with a spindly, box-shaped or neutral pelvis. Other evidences of the virilizing syndrome occur (see Chapter XX) It is doubtful whether hypopituitarism alone will give rise to obesity; probably involvement of the hypothalamus occurs in all such instances. Evans concludes that all obesity is alimentary in origin, the alterations of metabolism produced by diverse endocrine disturbances effecting less energy expenditure in relation to food assimilated

Localized Obesity Localized collections of fat in areas in which fat is normally stored may give rise to lipomas or lipodystrophies. These conditions may be unilateral or bilateral, painless or painful (adiposa dolorosa). The underlying disturbance in fat metabolism is not known

Leanness. The chief causes may be constitutional or endocrine in origin. The chief constitutional factors leading to loss of weight are inadequate nutrition resulting from faulty dietary intake or poor absorption secondary to intestinal disease, impingement of the thoracic duct by mediastinal tumors, and chronic debilitating states, such as prolonged fevers, tuberculosis, carcinoma, and the like (see Chapter II) The chief endocrine causes of weight loss are hyperthyroidism, diabetes mellitus, hypopituitarism (Simmonds' disease) and Addison's disease.

Musculature. Increased muscular development may occur in acromegaly, hyperthyroidism (in childhood), and virilizing syndromes. (See Chapter XX, p 951.) Decreased muscular development may accompany general weight loss as stated above, myasthenia gravis and certain neurologic disorders, and hypogonadal states.

Skin

Changes in the texture, consistency, moisture and color of the skin are associated with certain endocrine affections. Increase in thickness and marked dryness occur in hypothyroid states whereas the hyperthyroid state produces excessive moisture and flushed appearance. The skin of hypogonadal and hypothalamico-pituitary individuals (Frohlich's syndrome) is characteristically soft and child-like in texture, the so-called "peaches and cream" appearance Acrocyanosis and purplish, abdominal striae occur in instances of basophilism (Cushing's syndrome). Gray-brown

pigmentation of the skin is noted in specific endocrine disorders, as the patchy, irregular, brownish pigmentation (also mucous membranes) of Addison's disease, bronzing discoloration of hemochromatosis resulting from an unexplainable iron deposition, and dirty, brownish hue of the face associated with pregnancy (chloasma). Storage of lipoid substances in the skin of diabetics produces yellowish masses (xanthoma diabeticorum); entirely different in origin is the yellow coloration (xanthosis) of the skin of diabetics which cannot be explained as the result of lipemia. The endocrine implications of acne, vitiligo and eczema remain unsettled. (See also Chapter III.)

Distribution of Hair

The distribution of hair may be either in the order of excess (hirsutism) or sparseness. *Excessive hair growth,* especially in women, may assume masculine distribution, i. e., hair about the face, extremities, nipples, between the breasts, masculine umbilical ridge and pubic escutcheon, and about the back, which is suggestive of a virilizing syndrome due to basophil tumors of the pituitary, adrenal cortical hyperplasia or tumors, arrhenoblastomas, thymomas, and idiopathic factors, the last being much the commonest. Racial and hereditary factors should be considered.

Sparseness of hair may be due to the nondevelopment of the secondary sexual characteristics, e. g., hypogonadism, or to hypothyroidism.

Facies

The facial expression of certain endocrine syndromes is characteristic. (See also Chap. V, p. 122.) In *childhood hypothyroidism,* the facies is typically round or ovoid with broad nose, open mouth, protruding tongue, and thick, dry, waxy skin. In *adult hypothyroidism,* the facies is fat and masklike, the skin is thick and dry, eyebrows are sparse, palpebral fissures are narrowed, the lips thick and the tongue considerably thickened.

In *hyperthyroidism,* the facies is apprehensive, with an alert demeanor, staring eyes with or without exophthalmos, and a malar flush of the skin. In *acromegaly,* all acral bones undergo marked overgrowth so that the facies becomes markedly ovoid with protruding lower jaw, thick, coarse lips, blunt supra-orbital ridges and prominent zygoma, thick nose, hypertrophied maxillary bones and hexagonal shape to the head. The expression is stupid in character.

In infantile and juvenile *hypo-antuitarism* (Lévi-Lorain syndrome) the facies tends to retain the characteristics of the growth period at which further maturation slowed markedly, i. e., the facies is childlike, presenting a broad face, globate skull, rounded cheeks, small, recessive chin and crowded teeth.

Sexual Development

This is one of the most important components of the endocrine survey. Objective data concern not only examination of the external and internal genitalia but appraisal of the level of gonadal function as determined by evaluation of the secondary sexual characteristics and reproductive ability. This will be developed more fully in Chapter XX.

Extremities

The contour of the extremities has few general characteristics. Spade hands and feet are seen in instances of hypothalamico-pituitary disturbances

(Frohlich's syndrome). Progressive growth and enlargement of the hands and feet constitute one of the early manifestations of acromegaly. Short, coarse hands with fat, stubby fingers may be associated with hypothyroidism, whereas fine, fibrillating tremors of the extended fingers are suggestive of hyperthyroidism. The bones are small in instances of infantile and juvenile hypo-antuitarism and the hands are small, gracile and childish. In achondroplasia the extremities appear shortened as compared to the trunk, indicating a decrease in the maximum growth velocity of the extremities as compared to that of the trunk. Prominent muscular development in the female may suggest a virilizing syndrome.

Anthropometry

The fact that each organ or area of the body has certain optimum periods of growth activity enables one to evaluate statural alterations by taking

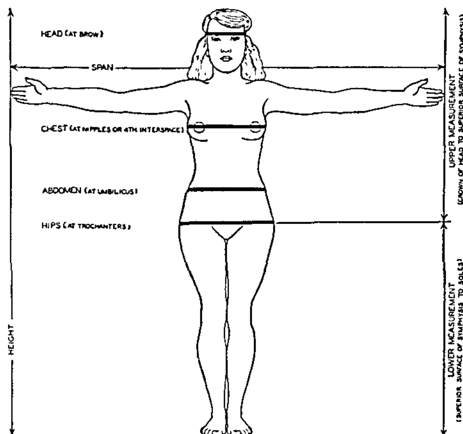


Fig. 585 Anthropometric measurements commonly taken in endocrinology. (From Hamblen, E C., Endocrine Gynecology, Charles C Thomas, Publisher)

certain anthropometric measurements (Fig. 585) and comparing with tables of minimal, maximal and optimal values (Figs. 586–589). Significant changes in these values are associated with classical endocrinopathies. Inasmuch as growth and development of the body as a whole embrace not only dimensional changes but functional alterations, i. e., a steady progressive matura-

NORMAL MEASUREMENTS IN RELATION TO AGE

AGE	HEIGHT (INCHES)				WEIGHT (POUNDS)				SPAN (INCHES)				UPPER MEASUREMENTS (INCHES)				LOWER MEASUREMENTS (INCHES)				CIRCUMFERENCE MEASUREMENTS (INCHES)					
																					HEAD		CHEST		ABDOMEN	
	M		F		M		F		M		F		M		F		M		F		M	F	M	F	M	F
	MIN	MAX	MIN	MAX	MIN	MAX	MIN	MAX	MIN	MAX	MIN	MAX	MIN	MAX	MIN	MAX	MIN	MAX	MIN	MAX						
BIRTH	19.3	21.1	19.0	20.8	6.2	8.6	6.4	8.6	18.1	20.1	18.1	19.9	12.1	13.1	12.1	13.1	6.9	7.9	6.9	7.9	13.9	13.6	13.8	13.6	13.4	13.2
1 MO	20.9	22.9	20.5	22.5	9.0	11.8	8.4	11.0	20.1	22.1	19.5	21.5	13.3	14.3	13.0	14.0	7.7	8.7	7.5	8.5	15.2	14.9	14.3	14.1	13.8	13.6
2 MOS	22.1	24.1	21.7	23.7	10.4	13.6	9.8	12.6	21.0	23.0	20.4	22.4	13.9	14.9	13.6	14.6	8.1	9.1	7.9	8.9	16.0	15.7	15.6	15.3	15.2	15.0
3 "	23.1	25.1	22.7	24.7	11.9	15.3	11.2	14.2	22.0	24.0	21.4	23.4	14.5	15.5	14.1	15.1	8.5	9.5	8.4	9.4	16.6	16.3	16.4	16.0	16.0	15.7
4 "	24.0	26.0	23.6	25.6	13.2	16.8	12.4	15.8	22.6	25.1	22.3	24.3	15.0	16.0	14.7	15.7	9.0	10.0	8.8	9.8	17.0	16.7	16.9	16.5	16.5	16.2
5 "	24.7	26.7	24.3	26.3	13.9	17.7	13.7	17.3	23.3	25.5	23.3	25.3	15.3	16.3	15.2	16.2	9.2	10.2	9.3	10.3	17.4	17.1	17.2	16.8	16.8	16.5
6 "	25.4	27.4	25.0	27.0	15.2	19.4	14.3	18.1	24.3	26.5	23.8	25.8	15.9	16.9	15.5	16.5	9.6	10.6	9.5	10.5	17.7	17.3	17.5	17.0	17.1	16.8
7 "	26.1	28.1	25.6	27.6	15.9	20.1	14.9	18.9	24.8	27.0	24.3	26.3	16.1	17.1	15.8	16.8	9.9	10.9	9.7	10.7	17.9	17.5	17.7	17.2	17.3	17.0
8 "	26.6	28.6	26.1	28.1	16.5	20.9	15.6	19.6	25.3	27.5	24.8	26.8	16.3	17.5	16.0	17.0	10.0	11.2	10.0	11.0	18.1	17.7	17.9	17.4	17.5	17.2
9 "	27.1	29.1	26.6	28.6	17.1	21.7	16.1	20.3	25.8	28.0	25.2	27.2	16.5	17.7	16.3	17.3	10.3	11.5	10.2	11.2	18.2	17.8	18.0	17.6	17.6	17.3
10 "	27.6	29.6	27.1	29.1	17.6	22.4	16.6	21.0	26.2	28.4	25.7	27.7	16.6	18.0	16.4	17.6	10.5	11.7	10.4	11.6	18.4	18.0	18.2	17.8	17.7	17.4
11 "	28.1	30.1	27.6	29.6	18.3	23.1	17.3	21.7	26.7	28.9	26.1	28.3	17.0	18.2	16.7	17.9	10.8	12.0	10.6	11.8	18.5	18.1	18.3	17.9	17.8	17.5
12 "	28.4	30.6	28.0	30.0	18.9	23.9	17.8	22.4	27.2	29.4	26.6	28.8	17.3	18.5	16.9	18.1	11.0	12.2	10.9	12.1	18.6	18.2	18.5	18.1	17.9	17.6
15 "	29.6	31.8	29.1	31.3	20.1	25.3	18.9	23.7	28.2	30.4	27.6	29.8	17.8	19.0	17.4	18.6	11.5	12.7	11.4	12.6	18.9	18.5	18.8	18.4	18.2	17.9
18 "	30.8	33.0	30.3	32.5	21.9	27.3	20.6	25.8	29.6	32.0	29.0	31.2	18.6	19.8	18.1	19.3	12.2	13.4	12.2	13.4	19.1	18.7	19.1	18.7	18.5	18.2
21 "	31.7	34.1	31.3	33.5	23.1	28.7	21.7	27.1	30.6	33.0	29.9	32.3	18.9	20.3	18.6	19.8	12.7	14.1	12.7	13.9	19.3	18.9	19.4	19.0	18.7	18.4
24	32.7	35.1	32.2	34.6	24.3	30.1	22.9	28.5	31.5	33.9	30.9	33.3	19.4	20.8	18.9	20.3	13.2	14.6	13.2	14.6	19.4	19.0	19.7	19.2	18.9	18.6
30 "	34.5	36.9	33.9	36.3	26.1	32.3	24.7	30.7	32.9	35.5	32.4	34.8	20.0	21.4	19.6	21.0	14.1	15.5	14.0	15.4	19.6	19.2	20.2	19.6	19.2	18.9
36 "	36.0	38.6	35.4	38.0	28.7	35.3	26.8	33.0	34.8	37.6	33.8	36.4	20.7	22.3	20.0	21.6	15.2	16.8	14.9	16.5	19.8	19.4	20.6	20.0	19.5	19.1
42 "	37.4	40.2	36.9	39.5	30.5	37.5	28.6	35.2	36.3	39.1	35.2	38.0	21.3	22.9	20.6	22.2	16.1	17.7	15.8	17.4	20.0	19.6	21.0	20.4	19.8	19.3
48 "	38.8	41.6	38.3	40.9	31.8	39.2	30.5	37.5	37.3	40.3	36.7	39.5	21.6	23.2	21.2	22.8	16.8	18.4	16.7	18.3	20.1	19.7	21.4	20.7	20.0	19.5
54 "	40.1	42.9	39.5	42.3	33.8	41.6	32.5	39.9	38.8	41.8	38.2	41.2	22.0	23.8	21.5	23.3	17.7	19.5	17.7	19.5	20.3	19.9	21.7	21.0	20.2	19.7
60	41.2	44.2	40.7	43.7	35.1	43.5	33.8	41.6	39.8	43.0	39.2	42.2	22.4	24.2	21.9	23.7	18.3	20.1	18.3	20.1	20.4	20.0	22.1	21.4	20.4	19.9

FROM ENGELBACH ENDOCRINE MEDICINE

Fig. 586. Normal anthropometric measurements taken in relation to age—from birth to fifth year (After Engelbach, W., Endocrine Medicine. From Hamblen, E. C., Endocrine Gynecology. *Charles C Thomas, Publisher*)

NORMAL MEASUREMENTS IN RELATION TO AGE

AGE	[illegible]
5.5 YRS	[illegible]
6 "	[illegible]
6.5 "	[illegible]
7 "	[illegible]
7.5 "	[illegible]
8 "	[illegible]
8.5 "	[illegible]
9 "	[illegible]
9.5 "	[illegible]
10 "	[illegible]
10.5 "	[illegible]
11 "	[illegible]
11.5 "	[illegible]
12 "	[illegible]
12.5 "	[illegible]
13 "	[illegible]
13.5 "	[illegible]
14 "	[illegible]
14.5 "	[illegible]
15 "	[illegible]
15.5 "	[illegible]
16 "	[illegible]
16.5 "	[illegible]
17 "	[illegible]
17.5 "	[illegible]
18 "	[illegible]
18.5 "	[illegible]
19 "	[illegible]
19.5 "	[illegible]
20 "	[illegible]

FROM E[illegible]

tion of the individual, anthropometric measurements are of value but do not alone permit diagnosis of the endocrine syndrome. These measurements should be incorporated into, and evaluated with, the clinical picture.

Normal Growth. A few generalizations about normal growth are in order at this time. In infancy, the face experiences the most sensitive alterations in growth. In the first five years of life, increases in the antero-

WEIGHT – HEIGHT – AGE TABLE FOR WOMEN

"IN ORDINARY STREET CLOTHES WITH OVERCOAT REMOVED"

AGE	4 FT 8 IN	4 FT 9 IN	4 FT 10 IN	4 FT 11 IN	5 FT	5 FT 1 IN	5 FT 2 IN	5 FT 3 IN	5 FT 4 IN	5 FT 5 IN	5 FT 6 IN	5 FT 7 IN	5 FT 8 IN	5 FT 9 IN	5 FT 10 IN	5 FT 11 IN	6 FT	AGE
20	106	108	110	112	114	116	119	122	125	128	132	136	140	143	147	151	156	20
21	107	109	111	113	115	117	120	123	126	129	133	137	141	144	148	152	156	21
22	107	109	111	113	115	117	120	123	126	129	133	137	141	145	149	153	157	22
23	108	110	112	114	116	118	121	124	127	130	134	138	142	146	150	153	157	23
24	109	111	113	115	117	119	121	124	127	130	134	138	142	146	150	154	158	24
25	109	111	113	115	117	119	121	124	126	131	135	139	143	147	151	154	158	25
26	110	112	114	116	118	120	122	125	128	131	135	139	143	147	151	155	159	26
27	110	112	114	116	118	120	122	125	129	132	136	140	144	148	152	155	159	27
28	111	113	115	117	119	121	123	126	130	133	137	141	145	149	153	156	160	28
29	111	113	115	117	119	121	123	126	130	133	137	141	145	149	153	156	160	29
30	112	114	116	118	120	122	124	127	131	134	138	142	146	150	154	157	161	30
31	113	115	117	119	121	123	125	128	132	135	139	143	147	151	154	157	161	31
32	113	115	117	119	121	123	125	128	132	136	140	144	148	152	155	158	162	32
33	114	116	118	120	122	124	126	129	133	137	141	145	149	153	156	159	162	33
34	115	117	119	121	123	125	127	130	134	138	142	146	150	154	157	160	163	34
35	115	117	119	121	123	125	127	130	134	138	142	146	150	154	157	160	163	35
36	116	118	120	122	124	126	128	131	135	139	143	147	151	155	158	161	164	36
37	116	118	120	122	124	126	129	132	136	140	144	148	152	156	159	162	165	37
38	117	119	121	123	125	127	130	133	137	141	145	149	153	157	160	163	166	38
39	118	120	122	124	126	128	131	134	138	142	146	150	154	158	161	164	167	39
40	119	121	123	125	127	129	132	135	138	142	146	150	154	158	161	164	167	40
41	120	122	124	126	128	130	133	136	139	143	147	151	155	159	162	165	168	41
42	120	122	124	126	128	130	133	136	139	143	147	151	155	159	162	166	169	42
43	121	123	125	127	129	131	134	137	140	144	148	152	156	160	163	167	170	43
44	122	124	126	128	130	132	135	138	141	145	149	153	157	161	164	168	171	44
45	122	124	126	128	130	132	135	138	141	145	149	153	157	161	164	168	171	45
46	123	125	127	129	131	133	136	139	142	146	150	154	158	162	165	169	172	46
47	123	125	127	129	131	133	136	139	142	146	151	155	159	163	166	170	173	47
48	124	126	128	130	132	134	137	140	143	147	152	156	160	164	167	171	174	48
49	124	126	128	130	132	134	137	140	143	147	152	156	161	165	168	172	175	49
50	125	127	129	131	133	135	138	141	144	148	152	156	161	165	169	173	176	50
51	125	127	129	131	133	135	138	141	144	148	152	157	162	166	170	174	177	51
52	125	127	129	131	133	135	138	141	144	148	152	157	162	166	170	174	177	52
53	125	127	129	131	133	135	138	141	144	148	152	157	162	166	170	174	177	53
54	125	127	129	131	133	135	138	141	144	148	153	158	163	167	171	174	177	54
55	125	127	129	131	133	135	138	141	144	148	153	158	163	167	171	174	177	55

FROM ENGELBACH ENDOCRINE MEDICINE

Fig 588 Weight-height-age table for women (After Engelbach, W, Endocrine Medicine. From Hamblen, E. C., Endocrine Gynecology. Charles C Thomas, Publisher.)

posterior and transverse diameters of the face predominate whereas increases in vertical growth are most vigorous after five years of life. This implies that brain-case growth is a function of infancy and early childhood, lower facial growth being more marked during adolescence and in the male than in the female The maximum velocity of growth of the extremities occurs during childhood whereas that of the trunk is pre-eminent during adolescence Statural growth of the female practically stops shortly after puberty whereas that of the male may continue for several more years. Puberty, therefore, delineates an important milestone in growth not only from the point of view of functional adequacy but from that of statural maturity.

WEIGHT – HEIGHT – AGE ———— TABLE FOR MEN
"IN ORDINARY STREET CLOTHES WITH OVERCOAT REMOVED"

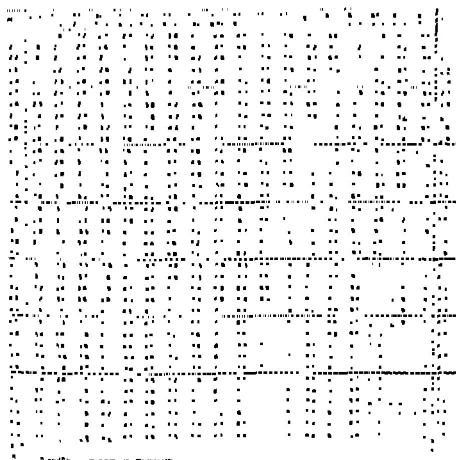


Fig 589. Weight-height-age table for men (After Engelbach, W., Endocrine Medicine, Charles C Thomas, Publisher.)

ROENTGENOLOGIC INVESTIGATION

of ossification and the times of epiphyseal closure. The classical studies of Engelbach and McMahon in 1924 defined the diagnostic applications of the osseous development, i. e., the appearance of diverse centers of ossification and epiphyseal union, to various endocrinopathies Generally speaking, endocrine disturbances in the rate of ossification are presumed to result from disturbances in function of the thyroid, gonads and pituitary gland. It is essential, however, to exclude constitutional disease.

The studies of osseous development find greatest clinical significance in children. If systemic disorders can be excluded, retarded osseous development in children is accepted generally to be a manifestation of hypothyroidism, either primary or secondary in origin, or hypopituitarism. After the age of puberty, retarded epiphyseal closure assumes additional clinical

importance as evidence of hypogonadism, either ovarian or testicular in nature. Acceleration of osseous development may be associated with precocious sexual maturity, resulting from ovarian tumors (chiefly the granulosa cell variety), hyperthyroidism, tumors of the adrenal cortex, pineal gland, or area of the fourth ventricle of the brain in that order.

The Skull. Roentgenologic diagnosis of diseases of the pituitary gland predicates the demonstration of alterations in the sella turcica as the result of lesions, chiefly tumors, intra-, or suprasellar in location. Considerable normal variation in the sella turcica may occur. Enlargement of the sella turcica does not necessarily suggest hyperfunction of the pituitary, nor does a relatively small sella indicate hypofunction of the pituitary.

Calcification of the pineal gland is not of especial clinical significance as this finding occurs in more than 50 per cent of normal adults. Instances of basophilism or hyperparathyroidism may reveal osteoporosis

Characteristic findings are observed in acromegaly which have been summarized by Hamblen, after Lisser, as follows· "(1) general hypertrophy of facial skull; (2) enlargement of pneumatic cavities (especially frontal sinuses), (3) prominent and widespaced malar bones, (4) enlargement and projection of the lower jaws (prognathism); (5) irregular thickening of the calvarium, (6) exaggeration of the external occipital protuberance."

Additional Roentgenologic Studies. Other roentgenologic studies may be pursued as the clinical evaluation of the case warrants Roentgenograms of the chest may demonstrate thymic enlargement or substernal goiter (see Fig. 140). Adrenal tumors may produce distortion in the renal calyces as revealed by excretory urograms or the adrenals may be visualized by injection of air into the perirenal spaces (see Fig 442). Utero-salpingography by air or with iodized oil finds especial value in studies of sterility.

SPECIAL LABORATORY STUDIES

In addition to the usual laboratory studies indicated in constitutional disease states, certain special laboratory procedures have confirmatory or complementary value in the endocrine survey.

Basal Metabolic Determination. As a measure of the rate of cellular oxidation, the basal metabolic determination is employed clinically for evaluation of the function of the thyroid gland The norm varies in different localities according to temperature, climate and other factors but is accepted commonly as ranging from minus 15 per cent to plus 15 per cent. There are a few additional physiologic variations which warrant consideration (Duncan). The newborn infant manifests low heat production and basal metabolic levels (approximately 25 calories per square meter of body surface), but the rate doubles within a few weeks. An increase in the rate of heat production ensues until the age of five years, whereupon the rate declines sharply from five to ten years of age, with a modest increase at puberty Between puberty and twenty years of age further decline of the rate of heat production is noted, but from the age of twenty years to senescence the rate of decline is gradual, with the exception of a mild increase during the climacteric of women. The basal metabolic determination of females averages 6 to 10 per cent lower than that recorded for males of the same age group.

Means lists the following causes for low basal metabolic levels: hypothyroidism; hypometabolism without myxedema; malnutrition; indirect alterations in thyrotoxic activity produced by hypofunction of the adrenals,

pituitary and pancreatic islets (diabetes mellitus); nephrotic syndrome; anemia, either pernicious or secondary in character; arthritides; peptic ulceration; and certain psychoses, neuroses and intracranial lesions To this list one should certainly add the effects of a warm climate and of a variety of drugs, chief of which are morphine, heroin, chloral hydrate, barbital, neonal, ipral and phanodorn.

High basal metabolic levels, on the other hand, indicate increased cellular activity such as may result from a variety of states, as hyperthyroidism, fevers, infectious disease, certain mental states with agitation, excitement or apprehension, blood dyscrasias, chiefly leukemia and polycythemia, certain neoplastic and wasting constitutional diseases, indirect alterations produced by hyperpituitarism (basophilism, acromegaly), manual occupations, stimulating climate, pregnancy (slight rise), and such drugs as caffeine, epinephrine and dinitrophenol

Lerman states that the basal metabolic level may be lowered to minus 40 to minus 45 per cent within sixty to eighty days following complete ablation of the thyroid gland.

Glucose Tolerance Curve. This test finds its greatest usefulness in the diagnosis of diabetes mellitus, the interpretation of the curve in other endocrine disturbances being variable The reader is referred to standard texts of metabolism for a discussion of this test.

Galactose Tolerance Curve. Althausen has described the galactose tolerance curve as being of significant value in the diagnosis of hyperthyroidism. The reader is referred to this source for details concerning this test. The studies of Rowe suggest that the assimilation limit may likewise be raised considerably in instances of hyperpituitarism but lowered in instances of ovarian failure.

Blood Cholesterol. This test, too, has confirmatory value in the diagnosis of thyroid disease, the blood cholesterol being lowered in hyperthyroidism and elevated in hypothyroidism, severe diabetes mellitus, xanthomatosis *and* von Gierke's disease.

Other Laboratory Studies. Endocrine diagnosis considers a large variety of blood chemical and urine studies, metabolic and tolerance tests, and hormonal methods (see Chapter XX) The reader is referred to standard texts of endocrine and laboratory diagnosis for listing of these procedures. Hamblen's monograph is recommended.

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XX

THE ENDOCRINE SURVEY OF SEXUAL AND REPRODUCTIVE SYSTEMS

The endocrine system manifests its most highly specialized and dominant functions in sexual and reproductive physiology. Pathologic alterations in endocrine activity result in diverse symptoms and signs which are associated with various degrees of impairment of the sexual and reproductive functions.

THE FEMALE

Normal Gonadal Function

An ability to diagnose normal gonadal function is a prerequisite to the identification of the abnormal; therefore, some of the various symptoms and signs which are associated with various epochs of normal gonadal activity are discussed. These normal data serve as points of reference in discussions to follow in regard to functional pathology.

Definition. This is done best by citing the varying manifestations of gonadal activity: (1) the production of an orderly process of sexual and somatic maturation during the adolescent epoch, i. e., from the sixth to the eighteenth years of age; (2) the induction of adequate uterine growth and development to permit an onset of estrogenic bleeding, the menarche, between the eleventh and sixteenth years; (3) the attainment by the sixteenth to eighteenth years of age of fairly regular ovarian and endometrial cycles which are characterized by the periodic discharge of fertilizable ova, by adequate prenidatory alterations of the endometrium and ultimately by terminal menstrual bleeding; (4) the maintenance, during the reproductive epoch from eighteen to forty years of age, of adequate fertility for the fulfillment of procreative aspirations and responsibilities; (5) the existence of sufficient reserve function to carry on effectively the added duties imposed by the gestational cycle and to permit uncomplicated recovery of short cycle menstrual functions after delivery; (6) the occurrence during the climacteric epoch from forty to fifty-five years of age of an orderly scaling down of activity which embraces the progressive loss of ovulational and progestational functions, the substitution of diminishing episodes of estrogenic stimulation and bleeding, and the eventual cessation of uterine bleeding, menopause, at an average of forty-six years; and (7) the initiation and completion of characteristic regressive changes in the sexual system during the postmenopausal phase of the climacteric.

DIAGNOSIS

During Premenarcheal Adolescence. 1. *Clinical Data Widening of the pelvis,* due to specific sexual characteristics in the growth of

the sacrum and innominate bones, and rounding of the hips, due to a local deposition of fat, occur often by the seventh to the eighth year and far in advance of the other signs of adolescence. Between the eighth and twelfth years the pelvic inlet is round or oval in shape; about the time of menarche it assumes its adult flattened trefoil shape. The beginning of these pelvic changes coincides with the recovery by the uterus of its original birth weight.

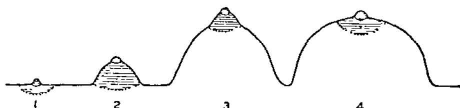


Fig 590. Various stages in the sexual differentiation of the breast, as described by Stratz. (From Hamblen, E C., Endocrine Gynecology, Charles C Thomas, Publisher)

The *mammary papilla* projects above skin level about three years of age. The breast remains in this juvenile state until the tenth or eleventh year, when the areola becomes elevated and forms, together with the papilla, a small conical protuberance this constitutes the bud or areola-

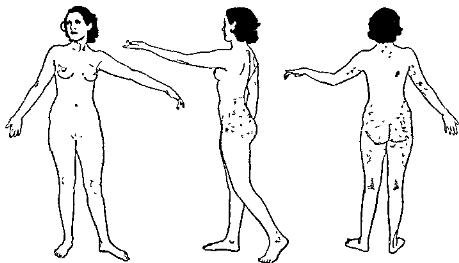


Fig 591 Physical and sexual signs of maturity The stippled areas show the localization of normal fat pads (After Farris, E. J Art Students' Anatomy, J B Lippincott Co) (From Hamblen, E. C, Endocrine Gynecology, Charles C Thomas, Publisher)

mamma stage As a rule, the primary mamma state is reached about the time of menarche. At this stage the papilla and areola are elevated by local fat depositions, the breast appearing as a "truncated cone situated upon the summit of a somewhat flattened hillock" (Greulich et al.) (Fig. 590).

...is first on

...eveloped;

...e.

These changes together with typically feminine localizations of *fat padding* form the gracefully curved body of the young woman (Fig. 591).

Mensurational data, especially those in regard to height, weight and certain body measurements (Chapter XIX), when correlated with age and referred to Standard Anthropometric Tables (Chapter XIX) permit significant deductions concerning somatic and sexual maturation.

The external genitalia show, in general, developmental stages compatible with the chronologic age Exact data are not secured but rather a general impression of how the individual compares with one's concept of normal is permitted. No standard tables for measurements of the external genitalia are possible due to marked individual variations

Bimanual abdominorectal or abdominovaginal examination and hysterometry (Fig 592), when possible, permit the assessment of cervicouterine growth and differentiation. A characteristic conversion of the cervico-uterine ratio or index from infantile to adult type begins about the tenth year of age and is completed by the seventeenth or eighteenth year (Fig 593).

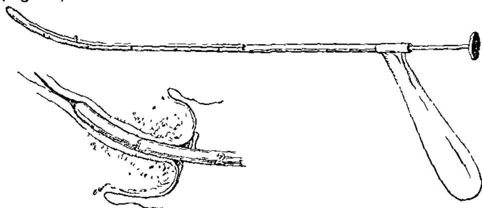


Fig 592 A modified uterine sound for hysterometric determination This instrument is similar to the one described by Meaker. The scale is graduated in fifths of inches (From Hamblen, E C, Endocrine Gynecology, Charles C Thomas, Publisher)

[illegible] and extreme individual variations render this direct method for assessment of ovarian function unreliable. The most rapid ovarian growth occurs between the ages of sixteen and twenty years.

Simple papular acne appears about the time of menarche and disappears normally about the time sexual maturity is reached.

Moderate enlargement of the *thyroid* may occur just prior to menarche. This normally subsides with attainment of maturity.

Normal psychosexual symptoms are associated with adolescence. Auto-erotic sensations (oral, anal and urethral), common during the circumnatal epoch, have disappeared by the time of onset of adolescence. A fleeting period of homosexual interest appears: this rarely expands beyond intensive girlish chumming, "crushes." It is a natural result of sexual awakening and the loosening of familial anaclinism. Soon auto-erotic and heterosexual interests appear: genital masturbation occurs. Self-consciousness and inferiority complexes appear: the individual wishes her hair were a different color, her complexion were better, her eyes were like a chum's, and the

like. The release from parental worship takes commonly the form of rebellion against discipline and tantrums when criticism is offered. Indecisions are frequent. Self control is difficult to maintain. Love affairs and daydreams of romantic natures evince sexual awakening

2. *Laboratory Data. Roentgenologic studies of secondary ossification centers and epiphyseal development, when correlated with age, yield valuable data upon the course of sexual development.*

About the time when the breasts reach the bud stage of development, the *chemical reaction of the vagina* changes from alkaline to acid and the dominant bacterial flora shifts from that of gram-positive cocci and diplococci to one characterized by gram-positive bacilli, the Bacillus vaginalis of Doderlein. Studies of vaginal smears or biopsies indicate the

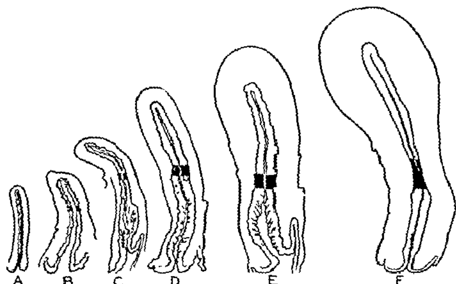


Fig. 593 Changes in the growth and development of the uterus and the cervix from the fetal to the adult periods The black band represents the level of the internal os *A*, Fetus of six and one-half lunar months *B*, child of two years, *C*, child of nine years, *D*, child of thirteen years (nonmenstruating), *E*, girl of fifteen years (menstruating), *F*, female of nineteen years (Adapted from Dickinson From Hamblen, E C, *Endocrine Gynecology*, Charles C Thomas, Publisher)

replacement of juvenile epithelial hypoplasia by adult-type cornification (Fig 594)

Average basal metabolic rates "peak" between the ages of ten and *fourteen years of age, the average value at twelve years being + 15 per cent.*

Creatine is excreted in good sized amounts in the urine of boys and girls until *sexual maturity is reached. The average daily excretion for* normal girls, average age 9.4 years, is 185 mg., for normal boys, average age 8.8 years, 142 mg (Bodansky and Bodansky). *Since these values are* reduced in hypothyroidism to one-half or one-third, studies may yield valuable data on gonadal function *Creatine excretion is slight or absent in the* normal adult male and minimal in the adult normal female. Since also the tolerance of patients to ingested *creatine varies strikingly with the stage of* sexual development, data from the creatine tolerance test are often sig-

nificant. Studies of urinary creatinine may yield valuable data upon m
cular growth.

	Estrogenic hormone →	Epithelium →	Glycogen →	Acidity →	Flora
Newborn	+		+	acid pH 4-5	sterile → Döderlein's bac. (secretion abundant)
Month old Child	−		−	alkaline pH 7	sparse, coccal and varied flora (secretion scant)
Puberty	appears		− to +	alkaline → acid	sparse, coccal → rich bacillary
Sex-Mature	+		+	acid pH 4-5	Döderlein's bacilli (secretion abundant)
Post-Menopause	−		−	neutral or alkaline pH 6-7	varied flora (secretion scant)

Fig 594. Biology of vaginal epithelium. (From Davis, M E., and Pearl, S A. Am. Jour. Obst. & G

Striking alterations occur in the *urinary excretion of various hormones* or their metabolic products. These permit the accumulation of valuable data in regard to levels of endocrine activity. Normal values for these endocrine excretionary products are summarized for reference in the assessment of the abnormal (Table 1).

Diagnosis at the Time of Menarche. *Hysterometric data* indicate usually that sexual maturity has not been reached: the adult cervico-uterine differentiation has not yet occurred.

Studies of the *endometrial proliferation* at the onset of bleeding add additional evidence in this regard: endometrium, secured by biopsy within the first twelve to eighteen hours after the onset of bleeding, is found upon microscopic examination to be in an interval or estrogenic stage and not in a progestational stage, indicative of antecedent ovulation.

No marked *psychic crisis* follows the first appearance of genital bleeding in the young girl who has had intelligent educational orientation upon sexual physiology.

TABLE 1

URINARY HORMONE VALUES (AVERAGED LIMITS OF RANGE) DURING PREMENARCHEAL ADOLESCENCE

Age in Years	Estrogens* mg./24 hrs.	Androgens* I U./24 hrs.	17-Ketosteroids† mg /24 hrs	Gonadotropin R U./24 hrs.
6-11	0 002-0.007	3-14	0 3-3.6	2-10

* Bio-assayable excretionary products extractable from hydrolized urine The "total" estrogens are expressed in terms of milligrams of estrone in which 1 mg. of estrone is equivalent to 10,000 international units, 1 I U of the urinary compound having the estrogenic activity of 0 1 gamma Androgens are expressed in international units of androsterone, 1 I U. of the urinary compound having the androgenic activity of 0 1 mg of androsterone

Although the urinary levels of androgens of girls do not demonstrate a cyclic variation, the levels of estrogens follow a cyclicity which begins approximately one and a half years prior to menarche (Nathanson, I T , L E Towne and J C Aub Endocrinology 28 851 1941).

† Colorimetrically determined 17-ketosteroids (alpha + beta) extractable from hydrolized urine. (The 17-ketosteroid estrone is removed from the urinary extract before estimation)

(*References to methods Estrogens* D'Amour, F. E , and Gustavson, R. G J. Pharmac. and Exper Therap *57* 472, 1936 *Androgens* Gallagher, T. F , and Koch, F. C. J. Pharmac. and Exper. Therap *55* 97 1935, McCullagh, D R and Cuyler, W. K.: J. Pharmac. and Exper Therap *66* 379 1939 *17-Ketosteroids* Callow, N H., Callow, R K , and Emmons, C. W · Biochem J. *32* 1312 1938, Talbot, N B., Butler, A. M , and MacLachlan, E. A . J Biol Chem *132* 595. 1940, Friedgood, H. B , and Berman, R. H.: Endocrinology *28* 248 1941 *Gonadotropins* McCullagh, D R , and Bowman, W. E.· Endocrinology *27*,525. 1940, Levin, L. Endocrinology *28* 378. 1941, Heller, E J , Heller, C. G., and Sevringhaus, E. L. Endocrinology *29* 1 1941)

Diagnosis during Postmenarcheal Adolescence. Since this epoch is terminated by the attainment of sexual maturity, i. e , the beginning of fertile ovario-endometrial cycles, significant diagnostic data establish this accomplishment.

1. *Clinical Data.* The occurrence of *relatively acyclic* and infrequent episodes of estrogenic bleeding for several years after menarche is not necessarily abnormal. Prolonged, excessive or too frequent bleeding is not normal.

Moderate menstrual discomforts, menorrhalgia, and severe menstrual pain, dysmenorrhea, usually do not appear as symptomatic associates of

bleeding until this becomes quite cyclic, i. e., until about the time of sexual maturity.

The *primary mamma stage* of breast development may persist into the adult epoch or the mature breast, the mamma papillata, may develop during this phase of sexual maturation.

Hysterometric data indicate the development of an adult cervico-uterine ratio by the seventeenth or eighteenth year of age.

Microscopic studies of endometrial biopsies secured at the onset of episodes of uterine bleeding will indicate the arrival of sexual maturity, i e., of fertile ovario-endometrial cycles, by the presence of fully differentiated progestational endometrial responses.

2. *Laboratory Data. Roentgenologic studies* of the epiphyses of long bones will indicate complete closure of all of these by the eighteenth year.

Studies of *urinary excretion* of hormones and hormonal products indicate the eventual attainment of levels of excretion of adult order (Table 2).

Diagnosis during the Reproductive Epoch. 1. *Clinical Data. Menstrual cycles* usually occur cyclically every twenty-six to thirty days. Flowing usually lasts three to five days. The first day of flowing is considered the first day of menstrual cycle. No woman is absolutely regular. Moderate variations in the cyclicity of flowing or in the amount of blood lost are not abnormal unless fertility is impaired. Infrequent ovario-endometrial cycles are not necessarily sterile cycles.

TABLE 2

URINARY HORMONE VALUES (AVERAGED LIMITS OF RANGE) DURING POSTMENARCHEAL ADOLESCENCE*

Age in Years	Estrogens mg /24 hrs	Androgens I U /24 hrs	17-Ketosteroids mg /24 hrs.	Gonadotropin R.U /24 hrs
12–15	0 008–0 025	26–58	5.0–9 8	2–11

* See footnotes to Table 1.

No symptoms are associated, as a rule, with *ovulation*. This usually occurs about fourteen days prior to the onset of menstrual bleeding. At times local ovarian pain and slight bleeding at this time of the cycle may indicate the discharge of an ovum. Scientific introspection of many patients leads them to believe they can recognize the time and site of ovulation.

The nonestablishment of an active libido and the absence of orgasm during coitus are not evidences of *deficient gonadal function*

Examination should reveal the existence of a state of *genital development* compatible with normal copulatory functions.

Whereas endometrial studies indicate the preponderance of progestational reactions at the onset of episodes of uterine bleeding, the infrequent finding of *estrogenic endometria* at the onset of bleeding does not warrant inferences that abnormalities of gonadal function exist. Normal women may interpolate infrequently a sterile cycle in their long series of fertile ones.

2. *Laboratory Data.* Studies of repeated *vaginal smears*, after suitable staining, reveal striking cytological variants which have been correlated with cyclic alterations in gonadal functions (Fig. 595). Investigations of

these may permit important inferences with regard to levels of gonadal function.

Cyclic variations are said to occur also in basal body temperatures, these variations have been correlated with changes in vaginal cytology and in gonadal function. Lowest basal temperatures are said to occur during the ovulatory or fertile cycle and about the time of ovulation.

The cyclic variations in the urinary hormones or hormone products of the normal adult woman are summarized for reference in the diagnosis of abnormalities of gonadal function (Tables 3, 4).

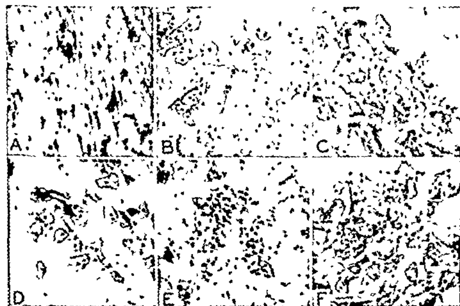


Fig 595 Cytologic alterations in the vaginal smears during the various phases of a menstrual cycle of a woman who menstruated regularly *A*, Third day of cycle many red cells, much fibrin and many bacteria *B*, Eighth day of cycle many epithelial cells, invasion of leukocytes into the body of these cells, increased number of leukocytes, little mucus, no red cells *C*, Thirteenth day marked decrease in leukocytes, increase in epithelial cells, many of which are cornified, little mucus *D*, Sixteenth day decrease in cornified cells, slight increase in leukocytes, much mucus and an occasional red blood cell *E*, Nineteenth day marked increase in leukocytes, some degeneration of epithelial cells *F*, Twenty-fifth day increase in epithelial cells, marked variations in shape and staining qualities, leukocytes decreased (From Hamblen, E C, Endocrine Gynecology, Charles C Thomas, Publisher)

Diagnosis during Pregnancy. During pregnancy ovarian function is amplified by the endocrine activity of the chorioplacental system. Accordingly, the apparent level of gonadal function is the sum total of ovarian and chorioplacental activities

1. *Clinical Data. Failure to menstruate* at the expected time is the common presumptive symptom of pregnancy Implantation of the fertilized ovum occurs about four days before menstruation is due. At times the *first bleeding after implantation is not postponed but, instead, a scanty* flow occurs which may arouse the suspicion of pregnancy. Occasionally, "implantational bleeding" may be of essentially the same order and amount

as a normal menstrual flowing and, thereby, a month's delay in the presumptive diagnosis of pregnancy may be occasioned.

Nausea and vomiting occur sufficiently commonly to be regarded by many as symptoms of pregnancy. These symptoms usually intervene before a second menstrual period is missed. Some workers have suggested that they result from an acute flooding of the system with the chorioplacental hormones.

Genital examination during the early stages of pregnancy and abdominal palpation during its latter stages yield clear-cut signs which permit the diagnosis of pregnancy and the assessment of its orderly, chronologic progress. These physiologic phenomena are made possible by the hormonal plethora supplied by the ovaries and the chorioplacental system. These clinical yardsticks for the diagnosis of pregnancy and for the evaluation of its course are described in Chapter XIII.

TABLE 3

URINARY HORMONE AND HORMONE PRODUCT VALUES (AVERAGED LIMITS OF RANGE) DURING THE FEMALE REPRODUCTIVE PERIOD*

Age in Years	Estrogens† mg /24 hrs.	Androgens I.U./24 hrs.	17-Ketosteroids mg./24 hrs	Pregnandiol‡ mg./24 hrs.	Gonadotropin† R.U./24 hrs.
18–40	0.008–0 16	25–61	5.4–16 1	28–57	5–24

* See footnotes to Table 1.

† Formerly, it was thought that in the excretion of urinary estrogens and gonadotropins, each reached a single "peak" just prior to ovulation. More recently, evidence has been presented which indicates two or more "peaks" in the urinary levels of these compounds during the menstrual cycle about midinterval, a few days before the onset of bleeding, and, in some instances, following the cessation of flow. As a result of rather liberal interpre- [illegible]

normal males (*References to methods* Venning, E. H.: J. Biol. Chem. *126* 595. 1938. Bucher, N. L. R., and Geschickter, G. F.: Endocrinology *27*·727, 1940)

2. *Laboratory Data* The *biologic diagnosis* of pregnancy is made upon the identification of large amounts of chorionic gonadotropin in the urine (Aschheim-Zondek or Friedman test). An outpouring of this gonadotropin begins when the fertilized ovum is implanted. It is possible, therefore, to diagnose biologically pregnancy even before a menstrual period is missed. Whereas these biologic tests are about 98 to 99 per cent accurate, false positives may be secured under a number of different circumstances.

The *normal urinary values* of the various hormones and hormonal products during the different stages of pregnancy, labor and the puerperium are summarized (Table 5, p. 940).

Diagnosis during the Premenopausal Climacteric. 1. *Clinical Data.* Symptoms or signs do not permit the assignment of an accurate date to the scaling down process of ovarian function which characterizes sexual aging. Certain of these, however, are important diagnostic landmarks.

As a rule, bleeding becomes progressively *less frequent and more*

TABLE 4

VARIATIONS IN VALUES (AVERAGED) OF URINARY ESTROGENS AND GONADOTROPIN DURING THE MENSTRUAL CYCLE

Days before bleeding	26	25	24	23	22	21	20	19	18	17	16	15	14	13	12	11	10	9	8	7	6	5	4	3	2	1
Gonadotropin MU/24 hrs *				30	30	30	20	7	12	12	15	23	22	12	13	13	7	7	7	8	21	20	12	12	5	5
Estrogens MUU/24 hrs *				35	35	35	20	3	5	5	17	19	14	16	12	8	13	23	28	28	32	22	22	22	7	7
Estrogens Mg /24 hrs †	017	012	0	066	0	029	025	03	036	05	062	043	051	032	033	038	031	037	036	031	037	025	011	011	015	004

* von Haam, E , and Rothermich, N O Proc Soc Exper Biol & Med 44 369 1940

† Gustavson, R G , Mason, L W , Hays, E E , Wood, T R , and D Amour, F E Am J Obst & Gynec 35 115 1938.

TABLE 5

URINARY HORMONE AND HORMONE PRODUCT VALUES (AVERAGED LIMITS OF RANGE) DURING PREGNANCY, LABOR AND THE PUERPERIUM*

	Months	Estrogens: Estradiol† mg /24 hrs	Estrogens: Estrone† mg /24 hrs	Estrogens: Estriol† mg /24 hrs	Estrogens: Total‡	Androgens I U /24 hrs	17-Ketosteroids mg /24 hrs	Pregnandiol mg /24 hrs	Gonadotropin R U /24 hrs
	1		0 025–0 05		0 025– 0 05		8 1	3– 11	150– 13,000
	2				0 52 – 0 20		6 7	4– 16	91,800–525,500
	3				0 099– 0 32		10 3	5– 26	25,800– 89,300
	4		0 4 –0 5	1 0	0 125– 1 43			6– 50	7,000– 27,800
	5		0 26 –1 0	5 0	0 193– 0 645			18– 60	1,870– 7,100
	6		0 63 –1 2	6 0– 7 0	0 888– 5 5	15		10– 70	3,000– 5,300
	7	0 11 –0 13	0 32 –0 96	4 0– 90 0	3 52 – 6 84	14		22–105	1,700– 4,900
	8	0 11 –0 14	0 37 –2 0	4 5–130 0	4 28 – 7 64	8–45		20– 95	1,830– 5,600
	9	0 014–0 22	0 8 –2 5	6 2–390 0	7 76 –28 64	13		25–150	2,250– 5,250
Days Antepartum	14	0 22	0 9 –1 65	25 0 222 0				43–124	
	12		0 5	12 0					
	10			115 0					
	7	0 125	0 8 –3 0	22 0–115 0				62–104	
	4		0 45	20 0				.	
	3	0 125	0 40					.	
	1	0 335	0 35–1 65	8 5 –13 5				97	
Hours of Labor	1	0 14	0 40	115 0				64	2,000–6,000
	2	0 085	0 85	9 0					
	3	0 135		3 2					
Days Postpartum	1		0 275	2 5				58–38	1,500
	2		0 225	3 0				25–15	300
	3							10– 4	120
	4							9– 1	0
	5		0 1	0 0					

* See footnotes to Table 1

† Hain, A M Edinburgh Med J *45* 678 1938, Smith, G V, Smith, O W, and Schiller, S Endocrinology *25* 509 1939, J Clin Endocrinology *1* 461, 1941

‡ The ranges for "total" estrogens in this column are derived from works in which no differentiation of the estrogenic principles in the urinary extracts was made, and are not to be confused with the totals of the three individual estrogens tabulated and which were obtained after fractionization of the urinary extract The apparent discrepancy between these totals is probably due in part to the various methods of extraction employed and to the difference in estrogenic activity between urinary estrone and estriol

scanty until its actual cessation at menopause. At times, menopause may occur abruptly and without any premonitory symptoms. Too frequent, *prolonged or excessive bleeding is abnormal.*

Various symptoms indicate a *disturbed vasomotor system*. The most common of these are the thermic vagaries, "hot and cold flushes," which have come to be regarded by some as being practically pathognomonic of the climacteric. These symptoms may be associated with many conditions other than those related to ovarian failure Neither the time of occurrence of irregular bleeding or of vasomotor instabilities bears a definite relationship to the onset of the climacteric.

Many *psychosexual symptoms* come into evidence during the climacteric. An active libido may lead to coitus with normal orgasm for years after the menopause and until regressions in the vagina impair its copulatory efficiency. The physiologic ovarian failure of this epoch does not entail frigidity. In fact, well past menopausal age, the vulvo-vaginal glands pour out their secretions under sexual stimulation. According to some clinicians (Hamilton), masturbation is common even during the seventh decade and cyclic variations in eroticism of lunar type may occur. Many women, however, may welcome the menopause as a valid excuse for release from long suffered and undesired sexual activity.

Much of the dread and many of the symptoms of the climacteric are due to misconceptions as to the normal significance of the epoch and to misinterpretations by woman of her own psychosexual symptomatology. Hamilton has summarized some of these as follows:

> "Many women find that, with the subsidence of the menopause, there comes a withdrawal of interest from environmental concerns, a dreary sense of unsatisfaction, preoccupations with gastro-intestinal and other bodily functions which may pass over into a more or less serious morbid melancholy and anxiety, sexual frigidity, a generally egoistic outlook upon life and a resultant unsympathetic, selfish, querulous attitude toward persons with whom they formerly sustained a more wholesome relationship They are easily offended, feel slighted when there is no adequate objective ground for this reaction, develop a host of petty grievances, expend a good deal of emotion on self pity and look for scapegoats onto whom they can project their inner self-dissatisfactions."

Various manifestations of *vasomotor instability* may be obvious upon examination dilated pupils, tachycardia, cold moist extremities, a labile blood pressure involving chiefly the systolic value, local hyperemias, dermatographia, and the like.

There is a tendency to *gain weight* due in particular to piling up of fat in the typically feminine areas, especially about the hips, the so-called "middle-age spread."

As a rule, significant *atrophic alterations* do not occur in the breasts and genital tract until considerably after menopause

Studies of *endometrial biopsies* taken at onsets of episodes of terminal irregular bleeding identify this bleeding as being estrogenic in nature, i. e , as ending non-ovulatory cycles

2. *Laboratory Data. Microscopic studies* of stained vaginal smears and investigations of basal body temperatures are said to identify also the terminal episodes of bleeding as being estrogenic in type.

Studies of *urinary hormonal levels* permit a graphic reconstruction of the endocrine alterations characteristic of this epoch. These data are summarized in Table 6.

Diagnosis during the Postmenopausal Climacteric. The postmenopausal phase of the climacteric has no finite end-point and passes imperceptibly into general somatic decadence. Its termination may be judged approximately by the attainment of a satisfactory subjective adjustment to the varied symptomatology of the climacteric.

1. *Clinical Data.* Marked variations occur in the rapidity with which *atrophic changes* occur in the sexual system. These changes are often masked in the breasts by local fat depositions although careful examination will reveal atrophic alterations in the areola and papilla.

Pubic and axillary hair becomes scanty. Hair of the head thins some but baldness does not occur as in the male. Some excess of facial hair may appear.

The *external genitals* decrease in size and become less succulent. Vulvar moisture decreases. The mucous lining of the labia minora and vulva appears pale and dry.

TABLE 6

URINARY HORMONE AND HORMONE PRODUCT VALUES (AVERAGED LIMITS OF RANGE) DURING THE CLIMACTERIC*

Period	Estrogens mg./24 hrs.	Androgens I.U./24 hrs.	17-Ketosteroids mg./24 hrs.	Pregnandiol mg./24 hrs	Gonadotropin R.U./24 hrs
Pre-menopausal	0.008–0 045	25–61	7.5–12.1	Occasional Normal Values†	67–167 R.U. (25–400 cc urine gives positive response.†)
Post-menopausal	0 0008–0 006		2 6–13 5	None	17–48 R U (10–30 cc. urine gives positive response ‡)

* See footnotes to Table 1.

† Since uterine bleeding is generally of estrogenic character during this period, pregnandiol excretion is not often encountered

‡ Heller, E. J, Heller, C. G., and Sevringhaus, E. L.. Endocrinology *29* 1. 1941.

Perineal muscles become hypotonic and relaxed. Descensus and prolapsus are common.

The *lumen of the vagina* is decreased in caliber and the vaginal fornices are obliterated The vaginal walls become relatively inelastic. The vaginal epithelium becomes atrophic. Studies of stained vaginal smears indicate usually a typical postmenopausal state, indicative of critical decreases in estrogen values.

The *cervix and uterus* decrease gradually in size until they are scarcely palpable by bimanual examination.

The *ovaries* become small and sclerotic.

2. *Laboratory Data.* The data upon urinary hormonal levels were summarized in Table 6.

Decreased Gonadal Function

Frequently by theory and too seldom by fact, the diagnosis of decreased gonadal function, or hypo-ovarianism, is made. Its existence is predicated

as a common cause of many functional disturbances of the sexual and reproductive systems.

Definition. Gonadal function is adjudged to be decreased when the usual orderly and chronologically related phenomena which are paramount to sexual efficiency, fertility and reproductivity are retarded, impaired or do not occur.

Time of Origin. The functional impact of hypogonadism is related to its time of origin. Deficient gonadal function may arise: (1) during adolescence; (2) during the reproductive epoch (intercurrent); (3) during pregnancy (intercurrent); and (4) during the climacteric (physiologic except when it occurs prematurely).

Grades. There are various grades of gonadal deficiency. Listed in progressive order of severity those truly ovarian in nature are: *simple gametopathic failure*, in which no impairment of endocrine functions exists although non-fertilizable or "blighted" ova are discharged; *relative progestin deficiency*, wherein ovulation and corpus luteum formation occur but the function of the corpus luteum is inadequate with regard to duration or level of function; *anovulatory failure*, which is characterized by the non-occurrence of ovulation and corpus luteum proliferation but which is not associated with any estrogenic deficits, and *estrogenic failure*, wherein there is not only failure of ovulation and corpus luteum function but also varying degrees of estrogenic deficiency.

During pregnancy, *intercurrent ovarian and chorioplacental failure* may occur; this is characterized by both estrogen and progestin deficiency.

Causes. The establishment of the cause of gonadal failure is necessarily a desirable part of any diagnostic survey. These causes may be varied. Failure may be due to causes *intrinsic to the ovaries*: developmental defects, fetal disease, injuries of various kinds, or functional disturbances may render the ovaries incapable of giving full normal responses to adequate stimuli from the pituitary.

The pituitary or the chorioplacental system in pregnancy may supply inadequate stimulation and a *hypogonadotropic* failure results.

Hypothalamic ovarian failure may result from lesions in the hypothalamus, which impair gonadotropic functions of the pituitary.

Deficient or excessive thyroid activity may upset gonadal functions through the medium of a disturbed metabolism alone or by way of alterations in the activity of the pituitary.

Impairments in the general level of health and nutrition may result in a *somatogenic type* of gonadal failure.

Neurologic and psychic disturbances may precipitate a *neuropsychogenic* type of gonadal failure.

The cause of gonadal failure may be *intrinsic* to the *uterus*. Organic pathology of the endometrium or myometrium or circulatory impairments of chorioplacental system may result in a *hysterogenic type* of ovarian failure characterized by disturbed production and metabolism of the sex steroids

Diagnosis of Simple Gametopathic Failure. The diagnosis is suspected when no cause can be discovered for sterility or repeated abortions in an apparently healthy couple When history indicates the existence of chronic intoxications of diverse sorts or of recent roentgenotherapy of the ovaries, the diagnosis rests on more secure foundations. Survey indi-

cates no evidences of an endocrine failure of the ovaries. Since no diagnostic methods are available for evaluating the adequacy of ova, an absolute diagnosis of this type of failure is not possible.

Diagnosis of Relative Progestin Deficiency. Symptoms include shortening of the menstrual cycle at the expense of the corpus luteum phase, "short luteal phase," and, perhaps, repeated early abortions probably due to a faulty implantational mechanism which results from inadequate progestational maturation of the endometrium. Studies of biopsies secured from the endometrium at the onset of bleeding reveal stages of immature progestational proliferation. Investigations of the daily pregnandiol excretion in the urine indicate a decrease in the duration and amount of this excretion. When this type of failure is corrected by curettage alone, the cause of it is assumed to have been one intrinsic to the endometrium. When injections of chorionic gonadotropin during the corpus luteum phase of the cycle are effective in restoring normal cycles, the cause is assumed to have been a hypogonadotropic one.

Diagnosis of Anovulatory Failure. *Adolescence.* Anovulatory bleeding is regarded usually to be physiologic during adolescence. Excessive, prolonged or too frequent estrogenic bleeding occurs fairly frequently during adolescence. The cause for these excesses of bleeding must be sought elsewhere than in the anovulatory cycles of the ovaries. Few patients with excess of bleeding exhibit any other obvious signs of endocrine disturbance. The fact that curettages often give temporary relief suggests that the endometrial vascular system may be at fault. A few patients present symptoms and signs of thyroid deficiency: low basal metabolic rates, retarded osseous age, elevated blood cholesterol, disturbed creatine tolerance, generalized obesity, moderately dwarfed stature, dry skin and hair and the so-called hypothyroid facies Occasionally bimanual examination identifies the presence of moderately enlarged cystic ovaries: these may suggest an undue sensitivity of the ovaries to pituitary gonadotropins or an excessive gonadotropic secretion by the pituitary. Hormonal studies do not indicate either a hypergonadotropuria or a hyperestrogenism under these circumstances.

Reproductive Epoch. Anovulatory failure is perhaps the most common form of ovarian disturbance during the reproductive epoch. It may be projected from adolescence as an instance of failure of complete sexual maturation or it may appear as an intercurrent complication caused by incomplete puerperal recovery or a premature climacteric.

The universal symptom is sterility. Uterine bleeding is most variable: it may be cyclic and indistinguishable in amount and duration from menstruation or it may be infrequent, too frequent, prolonged, excessive, scanty or absent. No evidences of estrogenic deficiencies exist: patients are well feminized and no genital hypoplasias exist. Studies of endometrial biopsies indicate a continuous estrogenic phase of proliferation. Pregnandiol excretion should be negative. Vaginal smears and basal temperatures suggest the absence of ovulatory cycles

A common cause of this type of failure is an intrinsic inadequacy of the ovaries: this inadequacy may have been primary or intercurrent. Hypothyroidism is an infrequent cause; when it occurs the usual signs and symptoms of hypothyroidism are present .Inadequate gonadotropic activity is predicated commonly to be a cause of this type of ovarian

failure; these patients show rarely any other symptoms and signs of pituitary deficiency. Studies of urinary gonadotropic levels have yielded no helpful data in these instances. When there is disturbed pituitary function, the occurrence of estrogenic failure of the ovaries and of symptoms and signs of secondary failure of other glands is anticipated. The fact that some patients recover normal ovarian function following substitutional therapy with ovarian steroids has suggested the possible existence of an endometrial causative factor.

Diagnosis of Estrogenic Failure. *Adolescence.* The universal symptoms during this period are failure or incompleteness of sexual maturation and nonoccurrence or delay in the onset of uterine bleeding. Accordingly, the severity and duration of estrogenic failure may be varied: it may result only in a temporary delay in adolescence or it may be projected into adult years, being characterized by permanent and cosmetically inelegant stigmata.

General clinical survey reveals usually the following signs: there is persistence of juvenile breast development and of a sexually immature body habitus; pubic and axillary crines are scanty or do not appear; osseous maturation is delayed, epiphyses remaining open, external and internal genitals retain their preadolescent size and differentiation; the vaginal epithelium, as judged by smears or biopsies, remains hypoplastic; the juvenile cervico-uterine index persists, urinary estrogens are low; urinary 17-ketosteroids are of preadolescent order.

When this grade of ovarian failure is related to *somatogenic factors,* history and examination usually are capable of relating the cause to wasting chronic illnesses, to cachexia due to errors of nutrition or to disturbances in metabolism.

When *deficiency in pituitary function* is responsible for the ovarian failure, other signs of hypopituitarism usually coexist· dwarfing of stature (Lévi-Lorain type); obesity (so-called Frohlich's type); signs of secondary hypothyroidism; localizing signs of pituitary or hypothalamic tumors; increased tolerance to glucose, increased urinary excretion of creatine, decreased urinary gonadotropins; significant roentgenologic changes in the sella turcica.

When the cause of the failure is one *intrinsic to the ovaries,* no signs of thyroid deficiency are present There is usually a spindly tallness which is due to overgrowth in the length of the extremities. There results a disproportion between span and height and between lower measurement and upper measurement. This overgrowth is permitted by normal pituitary growth functions which are unopposed by epiphyseal closures.

When estrogenic ovarian failure is *secondary to hypothyroidism,* the other usual symptoms and signs of thyroid deficiency coexist. Hypothyroidism is a relatively rare cause of this type of ovarian failure Adolescence may often occur somewhat prematurely in association with hypothyroidism.

Reproductive Epoch. During this epoch estrogenic failure may have two types of onset: it may have originated during adolescence and been projected into the adult epoch or it may represent an intercurrent complication, following a normal adolescence.

When estrogenic failure originated during adolescence, the same diagnostic symptoms and signs characterize its course during the reproductive

epoch. Epiphyseal closures, however, do occur eventually during the thirties regardless of the failure. Otherwise, unless altered by effective therapy, the deficient sexual maturation, absence or irregularity of bleeding and sterility persist.

Intercurrent estrogenic failure during the reproductive epoch is signalized by cessation of uterine bleeding, absolute sterility and the eventual occurrence of atrophic changes of postmenopausal order in the genital system and breasts. Accentuation of fat padding in the usual feminine areas is common, giving rise to a so-called "middle-age spread." Vaginal mucosa and endometrium, when studied by biopsies, are found to be atrophic. The cytology of vaginal smears is of hypo-estrogenic or postmenopausal order. Urinary estrogens are low; urinary 17-ketosteroids and gonadotropins usually manifest fairly well sustained increases, but eventually fall to essentially normal levels.

As a rule, intercurrent estrogenic failure results from causes intrinsic to the ovary: failure of recovery of ovarian responsiveness after the puerperium; premature aging of the ovaries; or damage from surgery or roentgenotherapy. Attempts at ovarian stimulation with gonadotropic extracts prove the existence of this intrinsic refractivity.

Hypothyroidism, although it may be a fairly frequent cause of anovulatory failure, rarely induces estrogenic failure.

Grave pituitary failure of the type observed in Simmonds' disease, late stages of acromegaly and in association with tumors of the pituitary or hypothalamus may result in intercurrent estrogenic failure. The characteristic symptoms and signs of this failure usually permit its causal relationship to the gonadal deficiency. Severe cachexia from malignancy or other chronic disease may produce estrogenic failure by way of functional alterations in the pituitary. Usually no difficulty is encountered in relating these somatogenic factors to the ovarian failure: the genital regressions are usually proportionate to the other somatic ravages of the primary disease.

After menopause and prior to well-advanced adolescence, estrogenic deficiency is physiologic.

Diagnosis of Intercurrent Ovarian and Chorioplacental Failure. Failure of the endocrine functions of the ovaries during the early weeks of pregnancy may result in abortion unless the chorioplacental system has reached a stage of development compatible with its carrying on alone these functions After the third month of pregnancy, the ovaries play a minor endocrine role in gestation, the major functions being exerted by the chorioplacental system from then until the end of pregnancy. Failure in chorioplacental functions is physiologic at the end of the ninth month of gestation and results in the onset of labor. Failure of this function prior to that time causes abortions, miscarriages and premature labors.

Intercurrent ovarian and chorioplacental failure, in addition to the obstetrical symptoms and signs of impending premature termination of gestation, is characterized by decreased urinary excretion of pregnandiol and estrogens. Pregnandiol excretion may be practically negative for some days before the uterus is emptied. As a rule, values of urinary gonadotropins do not show as strikingly early decreases as the steroids. Urinary 17-ketosteroids, being of adrenal origin, are not altered significantly in normal or complicated gestations.

Chorioplacental failure is commonly of intrinsic origin: faulty implantation (fibromyomas, ectopic pregnancy), endarteritis due to syphilis or nephritis, or faulty genesis due to "blighted" or abnormal embryo. In diabetes mellitus, even when this is treated adequately with insulin and diet, chorioplacental failure is fairly common during the latter half of pregnancy.

An early intrinsic ovarian failure before the chorioplacental system has become developed sufficiently to take over all the endocrine responsibilities of gestation may produce abortion. Deficient thyroid function is, perhaps, the most common endocrine cause of intercurrent ovarian and chorioplacental failure. Its causal implication is usually easy from the characteristic symptoms and signs of hypothyroidism.

Increased Gonadal Function

This is not of frequent occurrence. Certain symptoms, i. e., extreme eroticism, nymphomania, a high degree of fertility (especially if undesired by the patient) or an unusually striking state of feminization, may lead to an uncritical diagnosis of hypergonadism.

Definition. Increased gonadal function is said to exist when there occur quantitative enhancements in normal ovarian or chorioplacental activities or when disease produces an excessive secretion of some of the normal principles of ovaries or chorioplacental system but not a corresponding increase in total functional efficiency.

Time of Origin. The diagnostic symptoms and signs of increased gonadal function vary according to the time of its origin. It may occur during childhood, adolescence, the reproductive epoch, the climacteric, and during pregnancy.

Grades. There are several grades of increased gonadal function: *minor increases* in normal functions which may be either simple quantitative increases in ovarian activity (hyperovarianism) or simple quantitative increases in chorioplacental activity; and *qualitative excesses* of function due to disease which may produce either hyperestrogenism or chorioplacental hypergonadotropism.

Causes. Simple quantitative increases in *ovarian functions* may result from: intrinsic hypersensitivity of the ovaries; increased gonadotropic levels of pituitary function; hyperthyroidism, lesions in the hypothalamic area; or unusually good health, hygiene and nutrition.

Simple quantitative increases in *chorioplacental functions,* if they occur, are due to an increased volume of secretory tissue incidental to multiple pregnancies.

Hyperestrogenism results as a rule from granulosa cell tumors of the ovary.

Chorioplacental hypergonadotropism is associated with hydatidiform mole and chorio-epithelioma.

Diagnosis of Simple Quantitative Increases in Ovarian Function. *Early Adolescence.* There may occur precociously full sexual maturation during early adolescence. In these rare conditions true hyperovarianism, characterized by early maturing of the ovaries, may be considered to exist. This type of hyperovarianism is one of time rather than of quantity. Precocious maturity of this kind should be differentiated from premature feminization brought about by hyperestrogenism from granulosa cell tumors.

In addition to the signs of precocious feminization, the diagnosis of premature sexual maturity is founded upon signs that fertile ovarian cycles occur. Studies of endometrial biopsies taken at the onset of episodes of uterine bleeding should reveal the presence of progestational endometrial differentiation. Urinary studies should indicate the occurrence of normal adult cycles of estrogen and pregnandiol excretion. Roentgenologic studies should indicate epiphyseal closures to have been effected. Hysterometric data usually establish the existence of a normal adult cervico-uterine ratio.

Even in early stages of hyperovarianism of this type and before full sexual maturity is attained, differentiation of it from hyperestrogenism should be possible by studies of estrogenic values of the urine; these should be greater in the latter condition than those of a normal adult. Likewise, the identification of ovarian enlargement of greater grade than that of adult type should lead to a tentative diagnosis of granulosa cell tumor.

When precocious maturity is due to hypothalamic lesions, especially craniopharyngiomas or gliomas, neurologic symptoms and signs are usually present (Bailey). These may include symptoms of vasomotor instability (lability of blood pressure, sweating, flushing, "goose-flesh"), hyperthermia, voracious appetite, somnolency, pupillary irregularities, lacrymation, and the like. Childhood encephalitis may be followed by a hypothalamic type of pubertas praecox. Some workers have envisioned granulosa cell tumors as being capable of producing precocious maturity: such a concept is at variance with our concepts of hormonology. When no other causes are discoverable, it is assumed usually that fortuitous health and good nutrition working in conjunction with highly active and sensitive ovaries are responsible Differential exclusion of tumors from the latter innocuous circumstance is the primary responsibility and desideratum of diagnostic studies.

Reproductive Epoch The possible existence of hyperovarianism during this epoch is based upon high fertility indices, upon the frequent occurrence of multiple pregnancies and upon an increase in the duration of the reproductive span of years (i. e., deferment of climacteric changes).

Climacteric Years. During these years postponement of menopause well into the sixth decade may suggest prolongation of ovarian activity, i. e, hyperovarianism. Under these circumstances, the primary diagnostic responsibility of the clinician is to rule out by appropriate examinations the presence of malignant tumors of the uterus, cervix or ovary or hyperestrogenism due to granulosa cell tumor.

Diagnosis of Simple Quantitative Increases in Chorioplacental Activities. Certain elevations may occur in the functional status of the chorioplacental system in association with multiple pregnancies. Higher levels of excretion of pregnandiol, estrogens and gonadotropins are identified by urinary studies. These are due to absolute increases in the amount of functioning tissue.

Diagnosis of Hyperestrogenism. The most striking diagnostic signs of hyperestrogenism are yielded when it occurs during epochs of physiologic hypo-ovarianism, i. e., during childhood and early adolescent years and after the menopause.

Childhood and Early Adolescence. The universal symptom is premature sexual differentiation which does not proceed to full sexual maturation.

This condition may originate in the very early years of life. Usually rectal examination, under anesthesia if necessary, will reveal the presence of an ovarian tumor. Rarely bilateral tumors may exist. These tumors are usually firm in consistency, often of a degree comparable to fibromas. The degree and rapidity of the feminization induced vary. Studies of urinary estrogens reveal the values for these to be markedly increased, usually even far above normal adult levels. Occasionally the Friedman test may be positive (cause?) due to increases in urinary gonadotropins. Rectal or pelvic examination reveals genital hyperplasia commensurate with the obvious feminization. Irregular uterine bleeding occurs, investigation of which by biopsy indicates its association with various estrogenic proliferative phases of the endometrium. The "swiss-cheese" endometrial pattern is not infrequently present. A spurt in skeletal growth is associated commonly with the sexual differentiation but this does not result in undue tallness since early epiphyseal closures occur. The ultimate result is some dwarfing in statural height.

Reproductive Epoch. The diagnosis of hyperestrogenism at this time is difficult since the differentiation between normal estrogenic and excessive estrogenic effects is not easy Various types of irregular bleeding characterize hyperestrogenism. Investigation by endometrial biopsy of the bleeding [illegible]

failure induced by the excessive estrogenic levels A correct differential diagnosis may be reached by the identification of excessive estrogenic values of the urine and by palpation of a firm ovarian tumor on pelvic examination.

After Menopause. The return of uterine bleeding should arouse the suspicion of the existence of malignancy somewhere in the genital system: uterine corpus, cervix or ovaries. It is only when uterine and cervical malignancies have been ruled out by thorough studies that hyperestrogenism due to granulosa cell tumors should be considered.

If endometrial studies, always done by curettage when malignancy is suspected, indicate a considerable degree of estrogenic stimulation (*i e.*, endometrium is of hyperestrogenic or "swiss-cheese" type), there is likelihood that a granulosa cell tumor exists. Other signs of increased estrogenic activity usually are in evidence: increased vaginal secretion; vaginal smears of premenopausal type; biopsy evidence of adult-type vaginal cornification; increase in size and softening of internal genitals, fulness of breasts and erectility of the nipples. Studies of urinary estrogens often indicate values higher than those normal for a woman in the reproductive epoch. Pelvic examination may identify a firm ovarian tumor.

Diagnosis of Chorioplacental Hypergonadotropism. In chorionic disease, hydatidiform mole and chorio-epithelioma, there is an increased outpouring of hormonal substances. The obstetrical history and examination and careful pathological studies of available tissue are necessary for a complete diagnosis and for estimations of malignancy and invasive potentialities. Studies of urinary hormones are of little aid in these problems.

In hydatidiform mole and chorio-epithelioma, urinary values of gonadotropins are increased but these may not be in excess of those encountered in normal pregnancy at the time of the "peak" of their excretion, i. e , usually between the 30th to 60th day of pregnancy If repeated urinary studies indicate that this hypergonadotropuria continues for several months,

there is great likelihood that chorionic disease is present. Usually, however, by the time these studies can be completed, the differential diagnosis between chorionic disease and normal pregnancy has become obvious, usually on the basis of an abortion of a characteristic specimen or upon the basis of sure proof (the roentgenologic demonstration of the fetal skeleton) that a normal pregnancy exists. The securing of positive gonadotropin tests on spinal fluid is said to be reliable evidence for the existence of chorionic disease. At times the presence of large polycystic ovaries, "lutein cysts," may suggest the existence of chorionic disease.

Steroid metabolism, i. e., excretionary levels of estrogens and pregnandiol, have not been studied to any extent in chorionic disease. Significant alterations in these may exist and their recognition might permit an application in hormonal diagnosis.

In follow-up of the clinical course of patients who have had hydatidiform moles or in evaluating the effectiveness of treatment of chorioepithelioma, studies of urinary gonadotropic values are helpful. A persistently positive Friedman test under these circumstances is of poor prognostic import.

Intergrade Gonadal Function

Not all the disturbances in gonadal function are of a quantitative order, i. e., simple decreases or increases in function. Some are of a qualitative nature, i. e., they are characterized by intergrade functions or contrasexual inversions.

Definition. Intergrade gonadal function is said to exist when psychic, cosmetic or functional variations of a contrasexual order occur.

Time of Origin. The symptoms and signs of intergrade gonadal function vary with the time of origin of the functional disturbance. This may be: during childhood and adolescence; during the reproductive epoch; or during the climacteric.

Grades. There are several of these which vary in their endocrine significance: simple psychosexual states; simple hirsutism; hirsutism and virilization; and hermaphroditism.

Causes. The endocrine causes may include: masculinizing tumors of the ovaries; disease or tumors of the adrenals; and disease or tumors of the pituitary.

Diagnosis. *Simple Psychosexual States.* These include transvestitism (hermaphroditismus psychicus of Hirshfeld) and homosexuality (hermaphroditismus psychosexualis of Hirshfeld). In *transvestitism* an individual manifests psychic characteristics of the opposite sex. In *homosexuality,* sexual impulses are directed toward individuals of the same sex. Both these psychosexual states commonly occur in females who are characterized by no symptoms or signs of endocrine disturbance. There is normal feminization and the genital system is of isosexual order.

The pathogenesis and the diagnosis of the causes of these deviations lie within the province of psychiatry rather than in that of endocrinology. Since normal individuals of both sexes have bisexual hormonal patterns, qualitative tests for the presence of the contrasexual hormone yield no significant data. Whereas some workers have reported that hormonal studies indicate the existence of disturbed androgen-estrogen ratios in homosexuality, the ratio being disturbed toward that of the opposite sex,

sufficiently extensive studies have not been made to permit acceptance of these data as established facts.

Simple Hirsutism. Marked hirsutism may occur in women who exhibit no other symptoms or signs of endocrine disturbance, who even menstruate cyclically, and whose fertility and reproductivity are unimpaired. This hirsutism usually appears a few years after menarche and may increase gradually in amount. Since the psyche of these women is typically feminine, they suffer much anguish from their cosmetic inelegance. Despite this hirsutism being of masculine character and distribution, usually urinary hormone studies show no deviations from normal· values for estrogens, androgens and 17-ketosteroids may be of feminine order. Genital examination discloses no enlargement of the clitoris or regressive alterations in the sexual organs.

The cause of this hirsutism is not known It is obviously not endocrinopathic. It is probably due to genetic factors. Certainly we are not adherents to the beliefs of Albrecht, who some sixty years ago cited a greater frequency of hypertrichosis and a corresponding infrequency of baldness in women as some of the "proofs that the female sex is more persistently true to ancestral type, i. e., the closer to our savage forebears" (Ploss, Bartels and Bartels)

Hirsutism and Virilization. When hirsutism is but one of the symptoms of "defeminization" and masculinization of women, the endocrine nature of this disturbance is obvious.

Hirsutism and Virilization during Childhood and Early Adolescence. These virilizations produce most striking and severe alterations. At first there may be an abortive type of premature feminization some enlargement of the breasts may occur, the internal genitals may enlarge and there may be some irregular bleeding. Soon the masculinizing influences predominate: hair appears in the mustache and beard regions, about the breasts, on the thighs, legs and dorsum of the feet, over the shoulders and arms and over the sacral regions. Pubic hair appears and has a masculine distribution. The clitoris usually assumes penile proportions. The uterus decreases in size and bleeding ceases to occur The voice becomes husky and masculine in quality. Muscles become prominent (infant Hercules) or a plethoric type of obesity may ensue. There is change from the feminine hair-line of the head to one of masculine order, temporofrontal baldness appears and this may be followed by falling of hair from the vertex. There is statural growth but eventually dwarfing ensues due to premature epiphyseal closures. Dentition is advanced

Virilization during childhood and early adolescence is usually due to tumors or hyperplasia of the adrenal cortex Ovarian and pituitary virilizations usually appear during late adolescence or during the reproductive epoch.

Urinary values of 17-ketosteroids and androgens are elevated, markedly so when there is a malignant tumor of the adrenal. The presence of an adrenal tumor may be suspected from distortions in the kidney pelvis observed after pyelography. Perirenal air insufflation and roentgenography may outline the shadow of an adrenal tumor. When the tumor mass is large it may be palpated abdominally. The diagnosis is usually established by exploratory laparotomy, which the obvious symptoms and signs justify. Roentgenographic studies of the sella turcica should always be done

to rule out associated pituitary changes. The pelvic region should be examined for ovarian tumors at the time of adrenal exploration.

Hirsutism and Virilization during Late Adolescence and the Reproductive Epoch. Intercurrent virilization during these periods may be due to adrenal, ovarian or pituitary pathology.

The most striking sexual alterations occur from involvement of the adrenals. Menstrual irregularity occurs early and is followed soon by cessation of bleeding. The internal genitalia decrease markedly in size. The ovaries become small and sclerotic. The clitoris enlarges to penile proportions. Normal feminine hair distribution gives way to generalized masculine hirsutism. The normal feminine fat pads are resorbed and the body becomes angular. Muscles are prominent. Shoulders are broad. Voice is of male character. The skin becomes thin and acne and seborrhea are often troublesome. Breasts regress. At times a plethoric symmetrical obesity may occur. The psyche may become masculine: the result may be homosexuality. Not uncommonly weakness is present, together with other symptoms due to cortical deficiency: hypotension and pigmentation. Carbohydrate metabolism may be disturbed: hyperglycemia and glycosuria may occur.

The diagnostic methods, described in the preceding section on virilization during childhood, apply here. Roentgenograms of the sella turcica may help to rule out pituitary pathology. Exploration of both the pelvic and adrenal areas should be made.

Virilization due to involvement of the pituitary by basophilic invasion, basophilic adenomas or chromophobe adenomas (Cushing's disease) usually begins in late adolescence After some menstrual irregularities, amenorrhea occurs and pelvic examination reveals striking regressive changes in the genital organs. The clitoris, as a rule, is not markedly enlarged. A peculiar "buffalo" type of obesity develops· fat padding is localized chiefly to the torso and face and neck, the limbs appearing spindly in contrast. At times the obesity may be painful. A masculine mustache and beard which require shaving develop. There is a general hirsutism of male nature. The hypertrichosis is often not as great in amount as that seen when the adrenal is primarily involved. There develops frontotemporal and vertex baldness. Shoulders appear rounded and often, as a result, there is some decrease in stature The skin has a dusky plethoric appearance and purplish lineal atrophic areas develop. There may be hypertension, erythremia and osteoporosis, due to associated hyperparathyroidism. Hyperglycemia, glycosuria, fatigability and weakness occur.

Other less common symptoms and signs include: acrocyanosis, purpura-like ecchymosis, exophthalmos, visual loss from retinal exudate or hemorrhage, transient diplopia, albuminuria and nitrogen retention.

Roentgenologic evidence of distortion or enlargement of the sella turcica indicates pituitary involvement Negative roentgenologic data with regard to the sella turcica do not exclude pituitary pathology. Roentgenograms of the chest should be made, as very occasionally the syndrome may be associated with tumors of the thymus Negative diagnostic data with regard to adrenal involvement may emphasize the likelihood of pituitary pathology, although both may coexist. It is said that generally urinary values of 17-ketosteroids and androgens are less elevated than in the adrenal syndrome. Simpson has observed that if the clitoris be

TABLE 7

DIFFERENTIATION OF BASOPHILISM, CORTICO-ADRENALISM AND ARRHENOBLASTOMA*

Function	Basophilism	Cortico-adrenalism	Arrhenoblastoma
		Habitus and Circulatory Disturbances	
Obesity	Face and trunk	Face and trunk	Not characteristic
Purple striae	Usual	Usual	Rare
Ecchymoses	Common	Common	Absent
Rubicundity	Usual	Usual	Absent
Acne	Common	Common	Not characteristic
Hypertension	Present	Usual	Absent
		Metabolic Disorders	
Low carbohydrate tolerance	Common	Common	Absent
Osteoporosis	Common	Common	Absent
		Development and Sexual Functions	
Male			
Libido	Normal or diminished	Normal or increased	
Sexual development	Retarded	Precocious	
Female			
Libido	Normal or reduced	Normal or reduced	Normal or reduced
Menstruation	Abolished	Abolished	Abolished
Hirsutism	+	+	+
General function	Diminished	Masculinized	Masculinized
Genital organs	Normal or atrophic	Hypertrophy of clitoris	Hypertrophy of clitoris
Sexual development	Retarded	Precocious	Precocious
Children	Retarded epiphyseal union	Precocious epiphyseal union	Precocious epiphyseal union

* From Dorfman, Ralph I, Wilson, Hugh M, and Peters, John P., Endocrinology 27 2. 1940.

enlarged considerably and the skin is greasy and acneic rather than dry, a laparotomy to exclude adrenal tumor is justified.

The clinical course of virilization due to certain ovarian tumors (arrhenoblastomas, hypernephromas or adrenal tumors, including masculinovoblastomas) does not differ in kind from that described for the adrenal syndrome. As a rule the degree of virilization is not as marked. Differential diagnosis may be made upon the basis of outlining an ovarian tumor on pelvic examination. The pelvis should be investigated always for tumors when the adrenals are explored. (See Table 7.)

Hirsutism and Virilization after the Menopause. These virilizations do not differ materially in their course from those originating during the reproductive epoch, except that the menstrual symptoms are absent and the regressional alterations are far less striking. Some degree of hypertrichosis is not unusual after the menopause and this should not be confused with the syndromes under consideration.

Hermaphroditism. In hermaphroditism, genitalia and gonads of the two sexes are present in one individual. Embryologic faults rather than endocrine diseases are responsible. Ovarian hernia, hypertrophy of the clitoris in the female, and cryptorchidism and hypospadias in the male may simulate hermaphroditism. The gonads in these individuals may be either undifferentiated ovotestes or well developed functional ones characteristic of each sex.

THE MALE

The paucity of our knowledge of the sexual and reproductive physiology and pathology of the male warrants an apologetic preface. Engle has summarized the disparity between our data upon the female and male as follows:

> "For men no such definite landmarks as menstruation, pregnancy and menopause occur.
>
> "The endometrial and vaginal mucosa may be biopsied at any stage of the reproductive cycle, the ovaries are frequently observed at laparotomy. Perhaps 100 women have had their ovaries removed for every man who has been castrated
>
> "The internist, the surgeon and the psychiatrist record observations on the genital physiology and rhythmicity of the female in the course of routine medical examination. Aside from records of paternity, little information about the physiology of the male appears in medical charts. The gynecologist and obstetrician have become specialists in dealing with the normal as well as the pathological genital system of the female. For attention to the male genital system the only recourse is to the specialists in urology who have gained much knowledge of the pathology and surgery of the genital system but, in general, have not been interested in reproduction."

The most striking characteristic of the relatively few data available in andrologic physiology and pathology is their great degree of variability which concerns practically all phases of sex and reproduction.

Normal Gonadal Function

Despite the necessity for this apology in regard to the deficiencies of our knowledge, the same desirability of defining normal gonadal function exists in the male as in the female.

Definition. Normal gonadal activity varies during the course of three orderly physiologic epochs: (1) an *adolescent epoch* which is characterized by gradual proportionate skeletal and sexual growth and maturation, extending from the termination of the circumnatal period (infancy

and early childhood) at five to six years of age until full sexual maturity is established at eighteen to twenty-one years of age; (2) an *epoch of optimal fertility and reproductivity* extending from twenty-one to forty years of age and characterized by an effective potentia coeundi, by the ability to make a satisfactory sexual adjustment with a normal connubial partner and by the existence of a degree of fertility commensurate with the reproductive aspirations and responsibilities of the couple; and (3) an epoch of sexual aging, beginning about the fortieth year and characterized by diverse gradual alterations in the sexual and somatic systems.

DIAGNOSIS

During Adolescence. 1. *Clinical Data. Psychosexual data,* according to Hamilton, permit dating the transition from infancy and early childhood to the adolescent epoch (about fifth to sixth years)

He summarizes these characteristic personality changes as follows: increased preoccupation with ego satisfactions; decreased interest in auto-erotic sensual satisfactions (oral, anal and urethral); increased social interests and decreased familial interests; an increasing preoccupation with external reality; an expanding sense of adequacy to environmental demands; decreased anaclinism; and increased masculinity.

The personality changes of adolescence include impulses of rebellion against parental direction; the desire for adoption of the conventions observed by social contacts; a brief period of homosexual interest, characterized by sentimental chumships and resulting in no serious conflicts *unless older and more sophisticated associates take advantage of this vulnerability*; following this brief homosexual trend, auto-erotic and heterosexual interests appear; self-consciousness and inferiority complexes appear

Mensurational data, including those on height, weight and certain body measurements, when correlated with age and referred to Standard Anthropometric Tables indicate normal somatic and skeletal growth. These are good indices of sexual maturation

Direct inspection of the more important genital organs, being possible in the male, permits the securing of objective data on growth and development. The dimensional alterations in the testes and penis are recorded best by serial photography which circumvents errors incidental to manual manipulation necessary for direct measurements.

Testes descend normally into the scrotum during the last month of fetal life. During the circumnatal epoch and the early adolescent years, *the testes are ovoid or bean-shaped with a dorsal concavity. During infancy* the long axis of the testes is almost vertical Testes are firmer in consistency during the circumnatal period and early adolescence than during sexual maturity Little dimensional alteration occurs during the first decade An acceleration of growth occurs between ten and fourteen years of age. Extremely rapid growth begins at fourteen years of age; this results within a few years in an average five-fold increase in weight and a comparable one in dimensions.

As a part of this testicular growth, striking alterations occur in the epididymis-testis ratio At birth the epididymis constitutes 37.5 per cent of total testicular weight; at the fifteenth year, only 12 8 per cent. The left testis, which is the first to descend into the scrotum, is initially lighter but eventually becomes heavier. The extreme hyperplasia of the interstitial tissue, which occurs during the fetal period of growth, has regressed com-

pletely by the sixth year of age. By seventeen years of age the testes have attained essentially mature structure.

At birth the average length of the penis is about 2 to 2.5 cm.; at four years of age it is about 2.5 to 3 5 cm.; at seven years of age it is about 4.5 cm. Associated with acceleration of testicular growth, a rapid growth of the penis begins about *the tenth year of age. This growth concerns chiefly* the three corpora cavernosa.

The *width of the proximal end of the scrotum* is greater than that of the distal end up until the eleventh year. During the next few years there is gradual development of the adult scrotum in which the proximal end is narrower than the distal end.

The *breasts* may swell and become painful during the early years of the second decade when rapid testicular growth is occurring. At times, variable amounts of colostrum-like secretion may be observed. This stage in the breasts is a very transient one.

Pubic hair appears in most boys about the fourteenth year. The first hair develops immediately lateral to the base of the penis Axillary hair does not appear until about the fifteenth year when the pubic crines are

TABLE 8

URINARY HORMONE VALUES (AVERAGED LIMITS OF RANGE) DURING THE MALE ADOLESCENCE*

Age in Years	Estrogens mg /24 hrs	Androgens I U /24 hrs	17-Ketosteroids mg /24 hrs.	Gonadotropin R U /24 hrs
6–9	0 0005–0.0010	1–2	45–1 2	2–5
10–15	0 0007–0.0045	5–40	1 6–3 4	2–10
15–20	0 001 –0.0077	23–88	13.5–16 7	2–10

* See footnotes to Table 1

well developed. Terminal hairs develop on the upper lip about the time of appearance of the axillary hair.

The *voice change* usually occurs about the fifteenth year. The voice of the sexually mature male is said to be about one octave lower than that of the mature female (Greulich et al.).

2 *Laboratory Data. Roentgenologic studies* of secondary ossification centers and of epiphyseal development, when correlated with age should indicate normal sexual development. Complete maturity, as evidenced by closure of all epiphyses, usually has occurred by the twenty-first year.

On the average, *basal metabolic rates* show a "peaking" between the twelfth and sixteenth years of age, the average value at sixteen years of age being + 15 per cent.

The time of *disappearance of any appreciable amounts of creatine from the urine* may be a significant date line. This is said to coincide with completion of sexual maturation.

Seminal biometry should permit assessment of the time of full development of the spermatogenic function. Few of these data for this epoch are available. Microscopic examinations of morning urinary specimens of

adolescent boys thirteen years of age or older are said to reveal commonly the presence of spermatozoa.

Data upon the *urinary values* of various hormones or hormonal metabolic products during adolescence are summarized in tabular form for reference (Table 8).

Diagnosis during the Reproductive Epoch. 1. *Clinical Data.* Psychoanalysts describe characteristic psychosexual alterations which signalize the attainment of sexual maturity. Hamilton summarizes these as follows: decreasing self-consciousness; increasing self-confidence, a more serious, stable direction of vocational efforts; an increasing scope of gregarious interests; a trend towards altruism; a more habitual functioning with regard to realism; day-dreaming and other unrealistic responses are less frequent.

Sexual activity is, for the most part, of heterosexual character, although infrequent auto-eroticism is practiced throughout the reproductive period The sexual activity of the married male is extremely variable According to Peral (see Engle), it is not so much determined by age as by previous social, environmental and behavior patterns As a rule, the epoch of greatest sexual drive occurs during the third decade (twenty to twenty-nine years); this is followed by a gradual decline Greatest activity occurs in "farmers," less in "merchants and bankers" and least among "professional men."

Decreasing potentia coeundi is not necessarily associated with impairment of spermatogenesis or of potentia generandi. As a rule, however, marked decreases in fertility occur after forty years of age As being pertinent to this discussion, Engle cites data upon the ages of fathers at the time of the birth of their offspring: in 1934 in the U. S Birth Registration area, 3.8 per cent of births were to fathers forty-five to forty-nine years of age, 1.4 per cent to fathers fifty to fifty-four years, and 0 7 per cent to fathers aged fifty-five years and over.

Survey indicates the existence of the usually predicated *signs of masculinity:* a heavier, more developed and apparent musculature, larger and more prominent bones and less locally disposed adipose padding than in the sexually mature female; the barba and the sexual crines are typically distributed. Marked variations exist in the hirsute investment of the body and no correlation exists between it and the potentia coeundi The forehead hair-line of the sexually mature male is described as an inverted M-line whereas that of the sexually mature female, as well as of the immature male and female, is a bow-shaped line.

The *external genitals are of* adult dimensions. The penile prepuce is completely retractible or has been circumcised. Stimulation produces adequate erectility. Wide variations exist in the size of the erect penis and in the acuteness of the angle made by it with the symphysis pubis (Dickinson). The consistency of the testes is that of crepe rubber, not that of childhood firmness or of the doughy quality of sexual aging The left testis hangs lower in the scrotum than the right. The upper pole of the testis is directed slightly upward and laterally whereas the lower pole is directed backward and medially.

The *internal accessory genitals* possess a degree of development commensurate with functional adequacy. Rectal examination can define the normality of the prostate.

2. *Laboratory Data Biometric studies* upon freshly ejaculated seminal specimens, collected by auto-eroticism in clean containers, if possible,

rather than through the medium of condoms permit the securing of objective data regarding the onset of sexual maturity and the existence of adequate fertility. Since normal spermatogenesis is dependent upon normal endocrine activity, these data permit also significant deductions in regard to the internal secretory factors.

The usually accepted criteria for seminal adequacy are:

Average total volume of the ejaculate:	4.0 cc.
Average immediate purposeful motility of spermatozoa:	80 to 95 per cent
Normalness of cytology:	80 per cent or better
Endurance of spermatozoa at room or ice box temperature:	Majority motile after 24 hours
Number (average minimal):	60,000,000 per cc; 240,000,000 per total ejaculate
Average recovery time after coitus:	48 hours or less

These biologic properties are the result of a normal testicular spermatogenesis, adequate epididymal aging and normal fluid contributions by the seminal vesicles and prostate. These biometric data, despite their value

TABLE 9

URINARY HORMONE VALUES (AVERAGED LIMITS OF RANGE) DURING THE MALE REPRODUCTIVE PERIOD*

Age in Years	Estrogens mg /24 hrs.	Androgens I U /24 hrs.	17-Ketosteroids mg /24 hrs	Gonadotropin R U./24 hrs
21–40	0 0055–0 014	23–88	8 3–14 3	2–10

* See footnotes to Table 1

as measuring sticks of seminal function, do not establish, beyond peradventure, the existence of a normal fertilizing ability of the spermatozoa.

A *postcoition test* upon the female partner of the male permits assessment of his coital and ejaculatory functions. The finding of spermatozoa in the endocervical canal within the first hour after intercourse indicates normal delivery of spermatozoa.

Data upon the *urinary excretionary values* of various hormones or hormonal metabolic products during the reproductive period are summarized in tabular form for reference (Table 9).

Diagnosis during Sexual Aging. 1. *Clinical Data.* A consideration of the *psychosexual data* of the epoch is very important in regard to the nature and symptomatology of the so-called "critical age" or "male climacteric." A gradually decreasing potentia coeundi which begins after the fortieth year is the most universally accepted of the symptoms of sexual aging.

In view of the lack of positive evidence that sexual aging is due to a testicular failure comparable to the ovarian failure of women, any attempts at an evaluation of the symptomatology are worthwhile. The following psychoanalytic data are summarized from Hamilton.

The critical declines in potentia coeundi may result from psychical

reactions to the physiologically conditioned leveling-off of sexual potency. Support of this belief is lent by the responses of patients, who had reported complete absence of sexual desire and erections for five to fifteen years, to psychoanalytic treatments: erections, increased sexual desires, erotic dreams with nocturnal emissions; and resumption of masturbation if coitus is impossible. Factors which are judged operative in this psychical sexual repression include: a sexually inhibiting fear of complete loss of potentia; an increasing realization of sexual unattractiveness; more consciousness of somatic inadequacy; reversion to childhood fears of the dangerousness of sex; and frustrations which have resulted in attempts at coitus.

The inescapable intolerance and conservatism of the aging male, although time-honored and axiomatic, may be an expression of psychical sexual repression. Fearfulness of the ego's failure in this repression may explain the intolerance of the aged to any liberalization of social sanctions Disturbing dreams may reveal underlying fears of a break through in this sexual repression and give rise to vague sensations of groundless guilt and self-deprecations. Failures in this repression may result in the showering of amorous advances upon young girls and women, seeking the company of chorines and nightclub queens, or divorce and remarriage of a younger wife. This conservatism and intolerance, although usually able to withstand sexual stimuli, is notoriously vulnerable to the purveyors of promotional schemes, especially stocks in wildcat mines

Usual clinical examinations reveal no striking regressional changes in the *external genitals* of the male such as occur in the female There is some thinning of pubic hair and less resiliency of the testes. No appreciable decreases occur in testicular and penile dimensions.

Microscopic studies of testes secured at necropsy indicate little consistent evidence of impairment of spermatogenesis in the aged. Engle quotes data to the effect that spermatozoa were found in the testes of 68 5 per cent of men aged sixty to sixty-nine years, 59.5 per cent of those aged seventy to eighty years and in 48 per cent of those aged eighty to ninety years. He likewise found abundant spermatogenesis in more than half of the testes of men past seventy.

Similar studies in regard to the interstitial tissue indicate that the only constant change which occurs in association with old age is pigmentation. This is abundant in men past sixty years. It occurs in the interstitial cells, the efferent tubules of the testes, the smooth muscle of the prostate and in the seminal vesicles.

Opinion on the recognizable *gross dimensional changes in the prostate* varies. Engle quotes one observer as maintaining that no alterations in size occur normally from twenty to ninety years of age and another worker as reporting a

Microscopic

who is quoted

alterations:

1. Slight irregularities in the height of the epithelium are present at forty to forty-five years.

2 Lobular atrophy appears between forty-five and fifty years of age.

3. Loss of secretory activity of the glandular epithelium occurs between the fiftieth and sixtieth years

4. Sclerotic atrophy is apparent between sixty and sixty-five years of age.

5. Smooth muscle atrophy and stromal increase in fibrous tissue occur between the sixtieth and seventieth years.

6. After sixty-five years of age laminated corpora amylacea increase in number and size.

These changes in the prostate warrant dating the onset of sexual aging in the male at forty years of age. They indicate that the primary impact is on the prostate rather than on the testes.

2. *Laboratory Data.* Few data are available regarding studies of *ejaculates* of the aged. In view of the alterations which occur in the prostate, impairment of its contribution to the seminal fluid may result in significant alterations in volume and in activation of the spermatozoa. A well authenticated case of the occurrence of normal seminal values in a male of ninety-four years has been reported.

TABLE 10

URINARY HORMONE VALUES (AVERAGED LIMITS OF RANGE) DURING SEXUAL AGING OF THE MALE*

Age in Years	Estrogens mg /24 hrs.	Androgens I.U./24 hrs.	17-Ketosteroids mg /24 hrs	Gonadotropin R U./24 hrs
40–55	0 0007–0.0045	23–88	2.1–6 6	5–11
55 and over	0 0165–0 083	8–75		5–44

* See footnotes to Table 1

Data upon the *urinary excretionary values* of various hormones or hormonal metabolic products during sexual aging are summarized in tabular form for reference (Table 10).

Decreased Gonadal Function

The diagnosis of decreased gonadal function in the male is made all too frequently upon the basis of symptoms and without due regard for the presence or absence of objective alterations in sexual and reproductive functions.

Definition. Decreased gonadal function retards, impairs or prevents the usual orderly chronologically related phenomena paramount to sexual efficiency, fertility and reproductivity.

Time of Origin. The functional impact of hypogonadism is related to its time of origin. Deficient gonadal function may arise: during childhood; during adolescence; during the reproductive epoch (intercurrent); and during sexual aging.

Grades. There are two main grades of gonadal deficiency: androgenic (and seminal) failure; and simple seminal inadequacy.

Causes. The establishment of the cause of gonadal failure is necessarily a desirable part of any diagnostic survey. These causes may be varied. Failure may be due to causes *intrinsic to the testes:* developmental

defects, fetal disease, injury from trauma or disease, or functional nonresponsiveness to normal gonadotropic stimuli.

The pituitary may supply inadequate stimuli and a *hypogonadotropic* failure results.

Hypothalamic androgenic failure may result from lesions in the hypothalamus, which impair gonadotropic functions of the pituitary.

Deficient or excessive thyroid activity may upset gonadal function through the medium of a disturbed metabolism alone or by way of alterations in the activity of the pituitary.

Impairments in the general level of health and nutrition may result in a *somatogenic type* of gonadal failure.

Diagnosis of Androgenic Failure. *Childhood* Fetal pathology of the gonads may result in their inability to respond by interstitial cell hyperplasia to the chorioplacental gonadotropin; this may result in cryptorchidism. (Other causes of cryptorchidism are mechanical obstructions to descent and hypogonadotropic effects from the chorioplacental system.) Cryptorchidism, due to intrinsic failure of testicular response during the fetal period, is characterized subsequently by evidences of androgenic deficiency in adolescence. Subsequent examinations may identify atrophy of the testes. This type of intrinsic testicular failure is suspected when intensive gonadotropic therapy for cryptorchidism fails to bring about descent and also fails to indicate the existence of any obstructive factors (swelling and pain in the inguinal region without descent).

Adolescence. Androgenic deficiency of the male is suspected earlier than estrogenic failure of the female since hypogenitalism of the male is often apparent on inspection. The many variables of the normal male make errors in this regard common Frequently the genital dimensions of fat boys are underestimated, since their heavy pubic fat pads may conceal a considerable portion of their penile shafts. Retraction of these fat pads results in fewer diagnoses of adiposogenitalism.

In addition to producing hypogenitalism, adolescent hypogonadism is characterized by a delay in or a nonoccurrence of orderly sexual maturation. Pubic and axillary crines do not occur or are scanty. The voice remains childish in type. The beard does not develop sufficiently to require shaving The penis and scrotum remain juvenile in type. Erections and nocturnal emissions do not occur Heterosexual interest is minimal Potentia coeundi and potentia generandi are absent. The androgenic deficiency, itself, usually makes seminal studies impossible, impairment in spermatogenic function rightfully is assumed and it is established usually when it can be investigated.

When there is in evidence none of the definite signs of sexual maturation in males of late adolescent or adult years, the diagnosis of androgenic deficiency is an obvious one If there are postponements of two to three years in the time of occurrence of the various datable events of the orderly progress of adolescence, the existence of some degree of gonadal deficiency should be suspected. When studies of urinary androgen levels are possible, the finding of low values of these aids in the establishment of the diagnosis.

When examinations are made upon patients whose adolescent hypogonadism has been projected into adult years, the following findings, in addition to the obvious sexual ones, may be observed. a tendency toward hypotension and hypometabolism; evidence of disturbed protein

metabolism, indicated by decreases in nitrogenous excretion, the continued urinary elimination of relatively large amounts of creatine and the existence of a flabby, hypotonic musculature, which occasions deficient muscular power. Osseous epiphyses remain open far past the usual time for closure; closure is effected, however, regardless of whether or not treatment is instituted, during the fourth decade. Premature aging is common, the "peaches and cream" skin of the first two decades being followed in the third and fourth by a wrinkled, leathery geroderma.

When the cause of adolescent hypogonadism is one intrinsic to the testes, obesity and dwarfing of stature are rare. The fat padding is sparse, musculature poorly developed and the bones are frail and childlike. When this condition is projected into adult years, typical hypogonadal tallness results, due to the fact that the normal growth function of the pituitary is unopposed by epiphyseal closure. There results overgrowth of the long bones, which produces characteristic anthropometric variations: increase of span over height; increase of lower measurement (from soles of feet to top of pubis) over upper measurement (top of pubis to crown of head).

When hypogenitalism and obesity are associated, a common diagnosis is adiposogenitalism. Most endocrinologists predicate the primary lesion of this condition to be in the hypothalamus or about the pituitary stalk with projection along the pathways to the pituitary. Both the anterior and posterior lobes of the pituitary usually are involved. Neurologic studies, encephalography and skull roentgenograms in some instances may identify pituitary cysts or craniopharyngiomas; the majority of patients, however, shows no localized pathology. In adiposogenitalism, the obesity is particularly marked in the mammary and hip regions, the result being a typus femininus habitus The face is full. The hands are chubby and the fingers usually taper. Genu valgum and cubitus valgus are present. Hyperextensibilities of the knee and elbow are common. Moderate dwarfing of stature is not unusual. Diabetes insipidus may be present. Food intake generally has been quite excessive, particularly that of carbohydrates. The clumsiness of these patients is proverbial. As a rule, androgenic deficiency is not absolute, the result being tardy and incomplete sexual maturation.

Generalized obesity, dwarfing of stature and retardation in sexual development may result from hypothyroidism. This secondary hypogonadism is differentiated fairly readily from adiposogenitalism. Hypothyroidism of this severity usually begins during the first several years of life. Classical signs of it are usually present: the typical thyroid facies; the dry skin and hair; mental retardation; retardation in the development of the secondary centers of ossification; low basal metabolic values; disturbances in the tolerance for and excretion of creatine; and increased blood cholesterol values.

Hypogonadism may be associated with marked dwarfing of stature, absence [illegible] somatic [illegible] roidism. [illegible] rounded cheeks, crowded teeth and a broad face. The bones are small but normal development of secondary centers of ossification usually occurs. The differential diagnosis in these instances is between somatogenic causes (illnesses, undernutrition and vitamin deficiencies) and hypofunction of the anterior pituitary (Lévi-Lorain type). History usually permits this differentiation. Hypothyroidism may produce at times a similar picture

except that osseous retardation, disturbances in creatine tolerance and mental sluggishness may differentiate it. If adequate facilities exist for the quantitation of levels of pituitary hormones in body fluids, these studies are of extreme value in assessing the etiologic role of the pituitary in the various gonadal disturbances.

Reproductive Epoch Intercurrent androgenic failure, which occurs after an adequate adolescence, may not be apparent on a general survey unless some acute injury to the testes is obvious from examination or history, i. e , atrophy from disease, trauma, or roentgenotherapy or surgical castration.

Regressional alterations in the external genitals are not characteristic Decrease in potentia coeundi cannot be relied upon as an unfailing sign of androgenic failure. Engle cites ample data that even castration of men with previously well-developed libido sexualis does not produce invariable impotence. Decreasing potentia and regressive alterations in the prostate may suggest androgenic failure. Obesity of a typus femininus order is *common in late hypogonadism Seminal biometry indicates concomitant* germinal failure. Androgenic values in the urine are low As a rule, some hypometabolism occurs and there may be decreased nitrogenous excretion.

As a rule, if this failure is due to causes intrinsic in the testes, history will indicate these and physical survey will reveal varying grades of testicular atrophy.

Commonly this failure is somatogenic Illustrative is the hypogonadism which is associated with severe diabetes mellitus; usually, history and examination reveal other impairments of constitutional disease or malnutrition.

When intercurrent hypogonadism is due to hypothyroidism, the well-known symptoms and signs of this condition usually permit differentiation

When hypogonadism is due to hypogonadotropic activity of the pituitary, other evidences of pituitary disease should be apparent. When it is a part of the syndrome of pituitary cachexia, Simmonds' disease, the diagnosis is usually made without difficulty. When it represents a late stage of hyperpituitary giantism or acromegaly, the striking signs of these syndromes assure accurate diagnosis. The diagnostic signs of pituitary basophilism will incorporate usually the hypogonadism as a secondary effect of that condition. Tumors of the pituitary or about the pituitary may result in intercurrent hypogonadism Intercurrent hypogonadism rarely occurs from simple functional disturbances in the pituitary When it does, the diagnosis is suspected by responses to intensive pituitary therapy Studies of gonadotropic titers may aid in evaluating levels of pituitary function Glucose and galactose tolerance tests may be of some value in differential diagnosis.

Sexual Aging. Androgenic failure of the testes during sexual aging is not a characteristic phenomenon similar to that of estrogenic failure of the ovaries in woman Some gonadal failure, probably of intrinsic nature, doubtlessly occurs. Premature occurrence of failure of this order would involve the same diagnostic problems just described Whereas seminal failure is a concomitant of androgenic failure, the existence of the former is not proof of the latter since seminal failure without androgenic failure may exist.

As discussions of normal gonadal function have indicated, it is not possible to establish, with objective certainty, androgenic deficiency as

being the cause of the various psychosexual symptoms which are experienced by the aging male.

Diagnosis of Seminal Inadequacy. *Adolescence.* This is physiologic during most of adolescence. Whereas the interstitial tissue of the testes responds to adequate gonadotropic stimuli at all ages from the time of birth, the seminiferous apparatus requires a period of growth and differentiation before it is capable of functional responses. Data upon the time when normal spermatogenesis occurs are wanting. Most noxious influences, such as diseases, injuries and traumatism, which may injure spermatogenic functions during adolescence, also produce disturbances of androgenic functions.

Cryptorchid testes, uncorrected surgically, usually lose their power of spermatogenesis when adult years are reached, although their androgenic functions are not necessarily impaired. Intercurrent hypothyroidism may produce impairment of seminal function without any disturbance in the maturing functions of adolescence The other symptoms and signs of hypothyroidism usually assure its diagnosis.

Reproductive Epoch and Sexual Aging. Seminal failure without androgenic deficiency is diagnosed when, despite the absence of testicular atrophy and of prostatic regression and despite normal androgenic levels of the urine, there exists seminal inadequacy as judged by biometric studies of the fresh ejaculate. This inadequacy is manifested primarily by critical decreases in the absolute number of spermatozoa and, often in addition, relative increases in abnormal cytological forms. Since the volume of the seminal fluid is, to a great degree, due to prostatic and vesicular secretions, its decrease cannot be regarded as direct evidence of testicular failure. Likewise, decreases in motility of the spermatozoa may be due to causes other than faulty spermatogenesis.

It is difficult to establish hypogonadotropic factors as being causative of seminal failure alone: these should result also in androgenic failure The poor results which follow intensive gonadotropic therapy attest the likelihood of antecedent diagnostic errors.

Sexual overloading may produce this type of failure. Its operation is identified readily by repeated seminal studies after varying periods of sexual rest.

Somatogenic factors are possibly the most common cause of seminal failure. These may be numerous and many are not identified readily by history and examination. Some of them are: poor level of health due to chronic disease, undernutrition, vitamin deficiencies; chronic intoxications of various types, including alcohol, tobacco, sulfa drugs; persistent gametopathic effects of febrile attacks, and the like.

When hypometabolism or hypothyroidism is a factor in seminal inadequacy, it should be identified readily by its diagnostic signs.

No clear-cut data exist which justify the belief that a failure in gametokinesis is a striking phase in the aging of the male as it is in the female.

Increased Gonadal Function

This occurs rarely. Certain [illegible] genitalism, marked hirsutism o[illegible] to the assumption of the existence [illegible] gonadism.

Definition. Increased gonadal function is considered to exist when premature sexual maturation occurs, when hypersexuality and marked fertility exist, when the potentia generandi continues well into the advanced years or more commonly when androgenic excesses of function exist without evidence of concomitant increases in the seminal function.

Time of Origin. The functional impact of increased gonadal function is related to a great degree to its time of origin. This may be: during childhood; during adolescence; during the reproductive epoch; and during sexual aging.

Grades. There are two main types of increased gonadal function: *true hypergonadism,* in which quantitative increases occur in androgenic and seminal functions without any impairment in the quality and efficiency of these functions; and *hyperandrogenism,* in which there is excessive androgenic functioning of the testes or adrenals without enhancement of, and often actual failure of, spermatogenesis.

Causes. The establishment of the causes of these disturbances is a necessary part of any diagnosis. These may be varied: *tumors of the testes or hyperplasia of the interstitial cells* may result in excessive secretion of androgens. The usual tumor is an adenocarcinoma of the interstitial cells. (Chorio-epithelioma tends to produce feminizing effects: gynecomastia and even secretion of milk.)

Hyperactivity of the pituitary, giantism, acromegaly and rarely pituitary basophilism, may be causes. Often pituitary basophilism exerts feminizing influences.

Hyperactivity of the adrenal cortex, hyperplasia, adenomas or mixed tumors containing testicular cells, may produce hyperandrogenism.

Tumors and infections in the hypothalamic and thalamic areas may be associated with *pubertas praecox.* This effect is brought about doubtlessly by secondary alterations in the pituitary function.

Tumors of and inflammations in the region of the *pineal* may be rare causes of precocious sexual development Their modus operandi is by alterations produced in the hypothalamic centers and not by virtue of any intrinsic secretory activity.

General *somatogenic* factors, exceptionally good health and nutrition, may advance somewhat sexual maturation and, thereby, suggest the occurrence of hypergonadism.

Diagnosis of True Hypergonadism. This is quite rare. More frequent is hyperandrogenism.

Childhood and Adolescence. Hypergonadism is characterized by a precocious sexual maturation which progresses to actual sexual maturity and which results in premature but normal potentia generandi, i. e., true *pubertas praecox.*

The precocious sexual development is obvious on casual examination Skeletal and muscular growth is concomitant. Osseous advancement is of a mature status. Androgenic values of the urine are of normal order or even slightly in excess of normal. Sexual drive of an adult character results. Increased spermatogenesis being characteristic also, the seminal values are of normal adult nature

Exceptionally good levels of nutrition and health may advance the time of sexual maturation but does not produce true hypergonadism

Lesions in the hypothalamic and thalamic areas, when these are causes, are identifiable usually by their neurologic symptoms and signs.

When hypergonadism is due to hyperpituitary function, other signs of the pituitary disturbance, giantism, make diagnosis quite easy. Positive roentgenologic evidence of a pituitary tumor may exist.

Reproductive Epoch and Sexual Aging. Hypergonadism during the reproductive epoch usually is secondary to hyperactivity of the pituitary, acromegaly or pituitary basophilism. Increased androgenic and seminal values indicate hyperactivity of both testicular functions. Symptoms include increased sexual vigor and fertility. Some hypergenitalism may be present. The other characteristic signs of the pituitary syndromes will establish usually the pituitary as the primary factor in the development of the hypergonadism. When the syndrome originates late in the reproductive epoch the reproductive span of years may be increased.

Diagnosis of Hyperandrogenism. Most so-called hypergonadal states are due to hyperandrogenism.

Childhood and Adolescence. The majority of instances of so-called *pubertas praecox* do not lead to prematurely fertile individuals but, on the other hand, to individuals only prematurely sexed. Only the endocrine side of gonadal function is involved in hyperandrogenism, no enhancement, and often depression, of the spermatogenic function resulting.

The precocious sexual development and hirsutism, characteristic of the condition, are obvious even on superficial examination. The marked enlargement of the external genitals (macrogenitosomia) is often in strange contrast to the degree of statural differentiation. Osseous development and dentition are advanced. Whereas skeletal growth is rapid, the ultimate statural development obtained is usually less than that normal for an adult, due to premature epiphyseal closures. In some cases, muscular development may be striking (infant Hercules), whereas, in others, there may be a plethoric obesity. A childish psyche often persists. An indomitable sexual drive may produce a worrisome problem in the absence of usual adult inhibitions. Copulatory acts are possible but sterility is the rule, since there has been no precocious spermatogenesis. Androgenic values of the urine may be far in excess of those normal even for the adult male.

When the cause is a tumor of the testis, usual clinical examination will identify its presence. Chorio-epithelioma is associated with increased urinary gonadotropin values. These have been described as being of the order of 10,000 to 40,000 mouse units per liter. Other tumors, teratomas and seminomas, may be associated with an increased gonadotropuria; these, however, exert no striking endocrine effects.

When there is no obvious testicular pathology, the cause is usually of adrenal nature. Exceptional strength and inordinate muscular development may suggest adrenal involvement. A plethoric obesity may cause the adrenals to be suspected. Defects in the kidney pelvis apparent on pyelography and visualization of increased shadows in the adrenal areas following roentgenologic studies after perirenal insufflation may add confirmatory evidence of adrenal pathology. Studies of testicular biopsies commonly reveal degenerative and atrophic alterations in the seminal and interstitial elements.

Reproductive Epoch and Sexual Aging. Hyperandrogenism rarely results during these epochs. Its occurrence may be suspected when there arise increased libido sexualis and potentia coeundi associated with evidences of spermatogenic failure. The latter results from the pituitary depressing

effects of the excessive androgenic secretion, which is evidenced by abnormally high urine values of androgenic products. There may be increased hirsuties and muscular development when the adrenal is involved. When the cause is a tumor of the testis, clinical examination should reveal this.

Intergrade Gonadal Failure

As was observed in the discussion of the female, not all disturbances in gonadal function are of a quantitative order: some may be of a qualitative nature, i. e., are characterized by intergrade functions or contrasexual inversions.

Definition. This is the same as that given for the female.

Time of Origin. This may be any time during life, usually during adolescence and the reproductive epoch.

Grades. These include: simple psychosexual states; apparent feminization due to hypogonadal syndromes; true feminizing syndromes; and hermaphroditism.

Causes. The endocrine causes of true feminization include: chorio-epithelioma of testes; adrenal tumors or hyperplasia; and pituitary basophilism.

Diagnosis of Simple Psychosexual States. The discussion of these in the female applies equally in the male

Diagnosis of Apparent Feminization Due to Hypogonadal Syndromes. In the discussion of decreased gonadal function of the male, it was pointed out that a typus femininus appearance often resulted, e. g , in adiposogenitalism and
nizations should be contr
may characterize syndromes,

Diagnosis of Feminizing Syndromes. Pituitary basophilism, Cushing's syndrome, is rare in the male When it occurs, it usually results in some degree of feminization. It usually begins during adolescence. An adiposity of feminine type and distribution occurs. The voice may become high-pitched or it may fail to change if the syndrome begins early. Gynecomastia is common and the breasts may actually secrete. Libido sexualis *and potentia coeundi either do not develop or disappear Hypo*genitalism may persist or atrophic alterations in the genitals may ensue As a rule, there occurs the typical hirsutism characteristic of the syndrome in the female The other diagnostic signs have been discussed in the female.

A similar feminizing syndrome may occur rarely in the male from adrenal

Chorio-epithelioma of the testis may also produce feminization. This is, as a rule, characterized by gynecomastia and occasionally breast secretion. The diagnosis of this tumor has been discussed under increased gonadal function.

Diagnosis of Hermaphroditism. The discussion of this condition in the female applies equally to the male.

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By Edward D. Thomas and Clement A Finch

XXI

BLOOD

In this chapter it is our purpose to discuss the pathologic physiology, the signs and symptoms, and the routine laboratory procedures which together allow one to recognize the various diseases of the blood The blood and bloodforming tissue comprise an organ which is strikingly different from the other organs of the body in that a portion of it is fluid and the remainder is deeply buried in the bones. "Biopsies" of this organ are so easily performed that the physician tends to think in terms of laboratory studies on the blood. Laboratory tests should not be minimized, but the symptoms and signs, though often widespread and protean in character, should be of even greater importance and value to the clinician. The problem is difficult for one cannot say "these are the physical findings of blood disease" since the blood is distributed throughout the body, and its abnormalities may be reflected in disturbed function of nearly every tissue of the body. For this reason a discussion of the bedside diagnosis of hematological disease is almost a postgraduate course in physical diagnosis. An understanding of the pathologic physiology of the blood is of the greatest importance in the interpretation of the signs and symptoms observed It is our purpose to discuss only a few simple laboratory tests necessary for proper interpretation of these signs and symptoms

Anatomically, the blood and bloodforming tissues represent one of the largest organs in the body. It might arbitrarily be divided into three portions, as follows: First, the *bone marrow* where erythrocytes, leukocytes and platelets are produced It is a tissue of perhaps 1500 cc. which is capable of expanding by displacing the fatty tissue of the marrow when body needs dictate. Second, the *circulating blood*, characterized in health by well-defined levels of the red cells, white cells and platelets. Because of its rapid circulation through the heart and vascular system the average blood volume of about 5000 cc can be considered relatively homogeneous in consistency except for slight hematocrit changes in vessels of different sizes The third compartment is the *reticulo-endothelial system* and particularly *the spleen*. In both the normal and the diseased state one should always be aware of the balance between blood production by the bone marrow and blood destruction in which the reticulo-endothelial system plays an important role. The circulating blood is a passive reflection of the balance between these two processes Reduced levels of the circulating cellular elements giving rise to anemia, purpura or decreased resistance to infection may occur either as a result of decreased bone marrow activity or by excessive activity of the spleen and reticulo-endothelial tissues. Because in this system of production and destruction of red cells, white cells and platelets a defect in any one may exist as a separate entity, it will be con-

venient to discuss separately these three systems when considering their diseased states.

PATHOLOGIC PHYSIOLOGY BY SYSTEMS

Skin

The bedside recognition of anemia may be difficult, since from person to person skin color varies greatly. Therefore it is necessary to have an understanding of the various pigments which make up skin color. The color of the skin is due to reflected light, and is modified normally by five pigments: melanin, melanoid, carotene, oxyhemoglobin and reduced hemoglobin. Melanin and melanoid are dark pigments, but also have the property of scattering light in the skin, as does the turbidity of the skin itself. The phenomena of scattering of light in the skin tends to allow greater absorption at the red end of the spectrum while the reflected light, seen by the

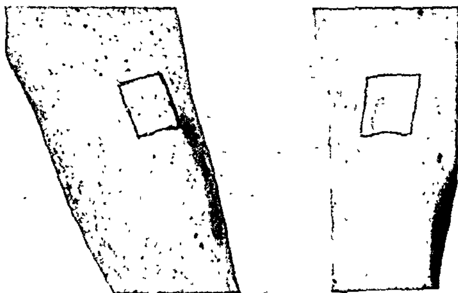


Fig 596 The appearance of petechiae following a tourniquet test in a case of thrombocytopenic purpura

observer, is accentuated toward the blue end of the spectrum. This is the reason for the commonly observed redness of light transmitted through the finger or ear lobe and blueness of blood seen by reflected light beneath the ski

skin. T

laries, i

at the arterial end and dark red reduced hemoglobin representing approximately 50 per cent at the venous end. Inspection of the blood through the skin will be altered by melanin obscuring the view, as in the dark-skinned races, and by the many physiologic and pathologic variations in the amount of blood flow through the skin.

An important sign of blood or blood vessel disease is bleeding beneath the skin. *Petechiae* are small subcutaneous hemorrhages ranging in size from those visible only with the aid of a small magnifying glass up to those of 2 to 5 millimeters (Fig. 596). *Ecchymoses* are common "black and blue"

spots of significance only when they appear without appreciable trauma. A *hematoma* is a large accumulation of blood in the tissue (Fig 597) *Telangiectases* are small red vascular dilatations in the skin which blanch when pressure is applied, best observed through a microscope slide. *Hemangiomas* represent a localized hyperplasia of vascular tissue and the common small cutaneous type has no significance These vascular abnormalities are to be distinguished from true hemorrhages in the skin.



Fig 597. A hematoma of the neck from hypoprothrombinemia due to overdosage with dicumarol

Bone and Joint

The marrow cavity of the bones is the site of manufacture of the blood corpuscular elements and because of this close anatomical relationship, changes in the bone marrow may be reflected by changes in the bones. This is particularly true in childhood because of the greater plasticity of the bones. Thickening of the diploe due to erythroblastic hyperplasia of the bone marrow produces the "hair on end" appearance of the skull x-ray in Cooley's and sickle cell anemia (Fig. 599) It should be remembered that normally, in the adult, bone marrow is not found in the distal extremities, but occurs in the "warm" areas in the proximal ends of the femora and humeri, and in the pelvis, vertebrae, ribs, sternum and skull. Consequently tumors associated with the bone marrow, such as multiple myeloma, will be found to produce osseous changes by x-ray or even pathological fractures in these areas (Fig. 598)

Joint disturbances in blood diseases are usually secondary to vascular disturbances such as purpura or a bleeding tendency, producing small or large hemorrhages into the joint, causing pain, and, if often repeated, eventual deformity and loss of function of the joint. Subperiosteal hemor-

rhages may produce swelling and tenderness and may be difficult to d
tinguish from the subperiosteal infiltration seen in leukemia.

Circulation

Acute blood loss produces a sudden decrease in blood volume and resul
in the syndrome of shock characterized by complaints of thirst, dull
consciousness, pale, cold perspiring skin, hypotension, and rapid threa
pulse. These symptoms are not due to a decrease in hemoglobin or oxyge
carrying capacity of the blood but are due to a failure of adequate bloo
flow to vital areas. In such instances the physician's efforts are directe



Fig 598. Extensive involvement of the proximal end of the femur in multiple myeloma

toward stopping the loss of blood and restoring the blood volume by means of transfusion.

In chronic anemias one is dealing with only minor changes in blood volume but with major changes in the circulating hemoglobin. The reduction in hemoglobin means that each unit volume of blood is not able to carry its normal amount of oxygen to the tissues and this deficit must be made up in other ways. One compensating mechanism of great importance is the circulatory system, which is called upon to circulate the available hemoglobin at a greater rate in order for the total amount of oxygen delivered to the tissue to remain the same. Cardiac output is increased.

Recent measurements by the technique of cardiac catheterization show a definite increase in resting output with a hemoglobin level of about 7 Gm 100 cc. and with a rapid increase in output with hemoglobin below that level The clinical evidence of this compensatory mechanism is reflected in the rapid heart rate with symptoms of palpitation, increased pulse pressure, and occasionally by capillary pulsation in the finger tips. Examination of the heart may show the presence of murmurs, usually systolic, blowing and not widely transmitted. Cardiac enlargement is not infrequently observed in anemia without other demonstrable cause

The added burden placed on the heart is partially relieved by a decrease in viscosity of the blood, lowered peripheral resistance, and increased oxygen utilization by the tissues. If the load on the heart becomes too great congestive failure may be superimposed with excessive dilatation of the heart, increased venous pressure, and edema. The oxygen supply to the



Fig 599. "Hair on end" appearance of the skull film in Cooley's anemia

Lymphatic and Reticulo-endothelial Systems

In an individual past puberty, easily palpable lymph nodes in other than the inguinal area usually indicate some pathological process. One should determine the size of the nodes, the presence or absence of tenderness, the consistency, and the presence or absence of matting together and fixation to adjacent tissue. Small, soft, non-tender nodes may be found in association with many types of febrile illness. Tender nodes indicate infection and resultant inflammation. The lymphoma group of diseases typically produce firm nodes of a "rubbery" consistency. Stony, hard, unyielding, bound-down nodes are typical of carcinomatous involvement.

In evaluating palpable lymph nodes it is most important to look for local skin abrasions or infections, since small lesions may occasionally produce a surprising degree of lymphadenopathy.

Enlargement of the spleen occurs in many conditions of widely varying nature such as leukemias, hemolytic anemias, cirrhosis, obstructive splenomegaly, and chronic infection. An enlarged spleen from a variety of causes may produce a decrease in the circulating level of any one or all of the cellular elements of the blood; this effect is known as "hypersplenism."

It remains to be shown that the spleen has any essential purpose. Although often mentioned as a storage place of blood readily available in case of emergency, recent experiments with red cells tagged with radioactive iron have failed to demonstrate any storage function in the normal spleen.

DISEASES OF THE BLOOD AND BLOOD-FORMING TISSUES

Diseases of the Erythron

The red-cell-forming tissue ranging from megaloblast to reticulocyte is located within the bone marrow and comprises some 250 to 500 cc. of cells. Each day it delivers about one tenth of its mass to the circulating blood.

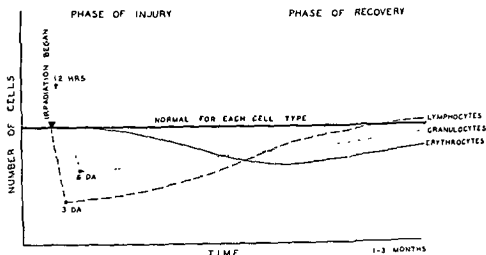


Fig. 600. Injury and recovery of blood cells after radiation therapy. *L* designates the curve of the lymphocyte count, *G* that of the granulocyte count, and *E* that of the erythrocyte count. (Dunlap, "Archives of Pathology," Vol 34.)

In the average individual the circulating red cells comprise some 2,500 cc. Erythrocytes are highly specialized for the purpose of carrying oxygen since they have no nuclei and consequently little respiration of their own, and contain almost the maximum possible concentration of hemoglobin. The life span of the average red cell is slightly over one hundred days so that approximately 1 per cent of the red cell mass is produced and destroyed daily. In view of this fact it is important to note that severe damage to

BLOOD PIGMENTS

Cyanosis is an abnormal blueness of the skin and mucous membranes becoming clinically evident when there is a concentration of approximately 5 grams of reduced hemoglobin per hundred cubic centimeters of blood circulating through the integument. Cyanosis may be due to a greater than normal extraction of oxygen from the circulating blood by the tissues as, for example, in the slow circulation of cardiac failure or in polycythemia More commonly it is seen in patients with heart or lung disease in which there is a decreased saturation of the arterial blood It is important to realize that cyanosis due to increased reduced hemoglobin will not be seen in the face of extreme anemia because of the reduction in the total amount of available pigment. Intense cyanosis may be produced by abnormal pigments such as methemoglobin and sulfhemoglobin in a concentration greater than 1.5 and 0.5 grams per 100 cc. respectively. These abnormal pigments may be differentiated by the fact that the patients do not change color on oxygen inhalation and, more important, when a blood sample is shaken in air for several minutes it fails to regain the bright red color of oxyhemoglobin These two pigments are intra-cellular pigments and are not in themselves associated with any abnormal red cell destruction

When the erythrocytes break down hemoglobin is split into the pyrol pigments, iron and globin. The pyrol ring structure is broken open giving bilirubin, a yellow pigment. *Jaundice*, or a yellow color of the skin and mucous membranes due to hyperbilirubinemia, occurs in several types of blood disease and is easily distinguished from hypercarotenemia (Plate I*B*) by the yellowness of the sclerae, since carotene has no affinity for scleral connective tissue. Bilirubin from excessive red cell destruction does not appear in the urine, whereas that due to hepatic disease or obstructive jaundice does. Pure retention jaundice, as seen in hemolytic anemias, is of a light yellow color due to bilirubin, while regurgitation jaundice tends to be more orange-green due to the presence of some biliverdin. Bilirubin is normally excreted in the bile and converted by intestinal bacteria to stercobilinogen and stercobilin, providing the normal brown color of the stool. Small amounts of it are re-absorbed in the intestinal tract and excreted in the urine as urobilinogen. In relating changes in pigment metabolism to blood destruction, it must be remembered that the liver has the important function of both excreting bilirubin into the bowel and also of handling most of the urobilinogen reabsorbed from the intestinal tract. In liver disease or obstructive jaundice the stools will be normal or light in c [illegible] will show bilirubin or excessive urobilinogen. In con- [illegible] the stools will be normal or more [illegible] [illegible]eased urobilinogen. [illegible] in the urine where it may [illegible] porphyrins.

GENERAL ANEMIA

Measurements of the oxygen carrying capacity of the blood is best expressed in terms of grams of hemoglobin per 100 cc. of blood, the normal value being approximately 15 grams per 100 cc. of blood. The measurement

in terms of concentration is justified since the important factor to body tissues and work load on the heart is the amount of available oxygen in each unit of blood. For purposes of *definition,* significant anemia may be said to exist when the concentration of hemoglobin is less than 12 grams per 100 cc. of blood.

In judging the degree of a patient's anemia good lighting is essential, daylight being preferable to artificial light. It is important to determine the degree of vasodilatation of the patient's skin, best estimated from the warmth of his exposed extremities, for the color depends to a considerable extent on the blood flow. Edema has a pronounced effect on the skin color, a common example being the pallor out of all proportion to anemia seen in patients with the nephrotic syndrome. In estimating the degree of anemia the physician should avoid as many of these variables as possible by observing the conjunctivae, creases of the palms of the hands, mucous membranes of the mouth, nailbeds and ear lobes.

Anemias developing rapidly produce symptoms with higher hemoglobin levels than anemias of insidious development. In the latter case a hemoglobin of 5 grams may produce few subjective symptoms, but in either case the severity of symptoms is related to the age of the patient, his daily activity, and the compensatory capacity of the *cardiovascular system* The first complaint may be shortness of breath on moderate exercise or simply extreme fatigability and lack of ambition. Other complaints based on the circulatory system may be pounding of the heart, angina pectoris

away from the skin to more vital areas. The physician may find a rapid pulse, increased pulse pressure, capillary pulsation in the fingertips, humming of the vessels of the neck, hyperactive heart sounds, systolic murmurs, sometimes a gallop rhythm and moderate cardiac enlargement. Flame-shaped retinal hemorrhages are found in severe anemias from any cause. Objective *neurological disturbances* are uncommon except in pernicious anemia, but the patient may complain of headache, dizziness, fainting, irritability, a roaring in the ears and black spots before the eyes. Pre-existing central nervous system lesions such as cerebral arteriosclerosis are exaggerated by the poor oxygen content of the blood and may result in disorientation and even psychosis. Vague *gastro-intestinal complaints* are common apparently resulting from poor oxygen supply to the gut. Dysphagia, lack of appetite, nausea, abdominal discomfort, flatulence and constipation are common to all types of anemia. Weight loss is not a common sign of anemia alone, but many conditions causing anemia may cause weight loss. *Menstrual disturbances* consisting of amenorrhea or menorrhagia may occur. It is worth noting that patients with severe anemia do not appear emaciated, but are often somewhat flabby with inelastic skin.

At the bedside one should be reasonably able to estimate the presence or absence of anemia. Then by the use of history, physical, and a few laboratory tests it should be possible to get an accurate idea of the nature of the anemia.

as to whether a normal, increased, or decreased amount of pigments were in it. The urine might show the presence of urobilinogen, bilirubin or hemo-

globin derivatives (hemoglobin is rapidly converted on standing to methemoglobin which is a fairly dark brown pigment in the urine). The hematocrit determination is particularly useful and is a very accurate way of estimating the red cell mass. It has the further advantage that one is able to see a buffy coat which represents the amount of white cells and platelets and the supernatant serum from which the icterus index can be calculated by comparison with standards. Thus in conditions in which blood destruction is increased, the icterus index will be elevated and the stools and urine will contain excessive blood breakdown pigments. In diseases associated with decreased blood formation such as infection, uremia and iron deficiency, the serum will be quite pale. With only a little practice one will be able to make an estimate of the size of the red cells as seen on the smear.

SPECIAL ANEMIAS

There are a great variety of anemias; those due to decreased blood production attributable to specific deficiencies or bone marrow dysfunction, those due to increased blood destruction and those due to blood loss Two types have specific patterns which will often allow their recognition at the bedside.

Iron deficiency is the most frequent of anemias In evaluating the history it is important to realize that iron is not excreted in any appreciable amount and therefore that iron deficiency *cannot* develop spontaneously or be produced by poor diet in the adult male Iron deficiency can develop through increased iron needs from growth, menstruation, pregnancy and lactation and in these circumstances adequate dietary iron is essential. However, blood loss is the most important cause of this variety of anemia. In history taking particular attention should be given to amount of menstrual bleeding, nosebleeds, tarry stools, bleeding hemorrhoids, etc The greater frequency of iron deficiency in the female is attributable to menstrual loss of iron. Anemia may produce the first signs and symptoms of iron deficiency and these have already been discussed. Chronic iron deficiency may produce a subjective sensation of extreme fatigue and objective epithelial changes such as spoon-shaped nails, and dry skin and hair Cheilosis, or cracking and fissuring at the corner of the mouth, may be seen and is indistinguishable from that seen in riboflavin deficiency Changes in the tongue include partial atrophy of the papillae and a glossitis characterized by irregular denudation of the papillae and irregular dusky red areas. The glossitis may be confused with that of pellagra except that the tongue does not have the typical bright red color Dysphagia may be produced by thin membranes in the upper portion of the esophagus. The Plummer-Vinson syndrome, characterized by stomatitis, dysphagia, and hypochromic anemia, is usually seen in women past middle life who have been on a diet containing an increased amount of milk. Chronic hypochromic anemia is often accompanied by achlorhydria and by loss of appetite and vague gastro-intestinal complaints The hematocrit tube will show a very pale serum and by smear the red cells are small, hypochromic and variable in size and shape. The variability in size and shape simply indicates that the bone marrow is working under difficulty, and it will be observed in many different types of anemia

Pernicious anemia is often insidious in onset and occurs usually after the age of forty Because of the slow development of the anemia it may be far advanced before the patient becomes aware of it. In addition to the

general symptoms of anemia, patients may complain particularly of numbness and tingling of the extremities and a sore tongue. Prematurely white hair, smoothness of the tongue along the borders (Fig. 88), and a pale "lemon yellow" color are typical of the disease. The latter finding is due to a combination of fair skin, pallor and mild jaundice This disease appears to be due to an inability to absorb adequately vitamin B_{12} from the gastrointestinal tract, producing an impaired synthesis of all blood elements. Achlorhydria is important in establishing the diagnosis. The hematocrit shows an icteric serum, a reduced buffy coat and on smear large erythrocytes, reduced platelets and hypersegmented granulocytes are seen. A distinctive characteristic of pernicious anemia is the associated finding of combined system disease, a degeneration of the lateral and posterior columns of the cord. In addition to the subjective sensory changes, patients complain of difficulty walking and particularly falling in the dark, irritability and bladder disturbances. Loss of vibratory sense in the lower extremities is common and the associated loss of position sense and absent reflexes produce incoordination on walking and a positive Romberg's sign If the lateral column lesions are prominent one may find some spasticity, increased reflexes, and a positive Babinski sign. Signs of peripheral neuritis are not uncommon

Cooley's anemia is a disease of the Mediterranean races In the classical type of the disease, the onset is insidious, usually being noted early in life. The typical child affected with this disease is small for his age. The skin has a pale brown-yellow color but frank jaundice is seldom present. The abdomen is prominent due to the enlarged spleen and often the liver. The cheek and frontal bones are prominent due to bone marrow proliferation and this plus the puffy eyes produce the "mongoloid facies." Mild forms of this disease occur in adults. The anemia is primarily one of decreased blood production.

There are two types of ***hemolytic anemia*** which may be distinguished by the pattern of blood pigment breakdown in each. ***Intravascular hemolysis*** designates destruction of the erythrocyte within the blood stream with liberation of free hemoglobin into the plasma Such intravascular hemolysis may occur as a result of many causes: among the more notable are malaria, B. welchii septicemia observed after abortions, fava bean sensitivity, chemical agents such as phenylhydrazine, mismatched transfusions, acute acquired hemolytic anemia and acute flare-ups of chronic hemolytic anemia Whatever the cause a characteristic syndrome is produced consisting of headache, malaise, backache, chills and fever, hemoglobinuria, jaundice and sometimes abdominal pain, prostration, and shock This may occasionally be followed by lower nephron nephrosis and anuria. Whenever one suspects intravascular hemolysis, blood should be drawn in a syringe coated with mineral oil, and centrifuged. One can easily detect 30 mg of hemoglobin per 100 cc. and thus demonstrate the intravascular hemolysis simply by inspection of the plasma. A level of around 150 mg. per 100 cc. must be obtained before hemoglobin is spilled into the urine. ***Extravascular hemolysis*** designates the increased destruction of red cells in the reticulo-endo-

the reticulo-endothelial system in this group of anemias, the spleen is considerably enlarged in most cases. Continued rapid blood destruction may produce signs and symptoms of cholelithiasis. Chronic leg ulcers are common in sickle cell anemia and congenital hemolytic jaundice. The continued stimulation to erythroblastic proliferation of the bone marrow brought about by blood destruction may lead to bone changes as previously mentioned.

In *sickle cell anemia* small punched-out areas seen in x-rays of the bones, particularly the hands, are presumably due to disturbances of local blood supply secondary to small thrombi formed by the abnormal red cells. Sickle cell anemia is worthy of particular mention because of its occurrence only in the colored race, because of the hemolytic and thrombotic crises in this condition which may simulate acute surgical abdominal emergencies, and because of the appearance of the erythrocytes when "sickling" preparations are made.

POLYCYTHEMIA

The term *polycythemia*, meaning an increased number of circulating erythrocytes (the upper limit of normal is approximately 5.5 million/cu mm. corresponding to an hematocrit of 50 per cent) has been applied to two conditions. The first, secondary polycythemia, is due to known causes, while the etiology of the second, polycythemia vera, is unknown

Secondary polycythemia of varying degrees is seen as a result of congenital heart disease, pulmonary disease, and the reduced oxygen tension of high altitude. The common denominator of all these conditions is a decrease in the total amount of oxygen delivered to the tissues. It would appear that the chief physiological stimulus to the bone marrow production of red cells in any condition is bone marrow anoxia.

Polycythemia vera is a disease of unknown etiology exhibiting an increased activity of bone marrow with elevated red blood cells, white blood cells, and platelets, and enlarged total blood volume. As a rule symptoms do not appear until the disease is well established, and they would appear to be due to an increase in blood volume and are similar to chronic mountain sickness Patients may consult the physician because of headaches, dizziness, weakness, dyspnea, peripheral vascular disturbances or symptoms of coronary artery disease. Coldness of the extremities is presumably due to the long circulation time. The increased volume of blood with increased number of red cells causes a dusky plethora best observed in the face, extremities, or mucous membranes. The eyes frequently look bloodshot due more to the increased blood volume with distention of the superficial vessels than to the high hematocrit itself The skin may show ecchymoses. In contrast to secondary polycythemia, the fingernails do not show clubbing. Skin hemorrhages are common The increased blood volume with increased hematocrit causes an increase in blood viscosity and this, with the high platelet level, results in a tendency to form thrombi. Thrombosis and varicosities in the veins of the legs are seen frequently There is often advanced arteriosclerosis and cerebrovascular accidents or coronary thromboses are a frequent cause of death. Angina pectoris is also common. Splenomegaly occurs in over two thirds of the cases, occasionally achieving very large size. The incidence of peptic ulcer is approximately four times normal. Bleeding from these ulcers as well as epistaxis is not unusual. Of importance in differentiating polycythemia vera from secondary polycythemia is the increase in

the level of white cells and platelets, easily observed by the increase in the buffy coat of the hematocrit tube.

Diseases Involving the Leukocytes

AGRANULOCYTOSIS

Agranulocytosis is a disease characterized by disappearance of circulating polymorphonuclear leukocytes from the blood with consequent loss of one of the body's main lines of defense against bacterial invasion. The illness is typically preceded by a day or two of weakness and fatigue, leading to extreme prostration, chills, high fever and an overwhelming necrotizing sepsis of the gums, pharynx and respiratory tract. One may often differentiate agranulocytosis from infection by a virulent organism by the involvement of gum margins in the former condition. Drugs are a common cause of this condition, the leading offender being amidopyrine, and others including sulfonamides, barbiturates, and thiouracil. Radiation injury produces granulopenia as well. Some cases of unknown cause have recurrent mild cycles of the disease. Whereas agranulocytosis in the presence of a large spleen usually means leukemia, there are cases of "splenic neutropenia" in which the spleen is responsible for the marked granulopenia. With the increasing use of atomic energy and radioactive materials agranulocytosis may become of increasing importance.

LEUKEMIA

The leukemias are a group of diseases characterized by widespread proliferation of the leukocytes and their precursors in the tissues of the body. The etiology is unknown but is generally presumed to be a neoplasm of the white blood cells. The leukemias are usually classified according to the cell type involved, but clinically the various types are quite similar. The best classification seems to be the division into acute and chronic types.

The *chronic leukemias* develop so slowly that the first complaint may be referable to the severe anemia as discussed previously. Patients may consult a physician because of weight loss, a bleeding tendency or symptoms produced by an enlarged spleen or lymph nodes. In chronic myelogenous leukemia enlargement of the spleen is usually present, often to great size. Some lymphadenopathy may be present, but usually it is of minimal degree. In chronic lymphatic leukemia lymphadenopathy is common, the glands being non-tender and freely movable and rarely of great size, while the spleen is usually moderately increased in size and is not necessarily palpable. Infiltration of the skin by leukemic cells has already been described. Patients may complain of loss of appetite, diarrhea, abdominal pain (due to infiltration of the gastro-intestinal tract by leukemic cells), gastro-intestinal bleeding, hematuria or excess menstrual bleeding (due to secondary thrombocytopenia). In a suspected case of leukemia tenderness over the [illegible]

[illegible] engorgement of the veins, blurred disks and hemorrhages; the latter occasionally show a white nodule of leukocytic infiltration in the center.

Acute leukemia may be called to the patient's attention by symptoms of weakness, pallor, bleeding, fever or sore throat. Lymphadenopathy may

or may not be present initially but cervical adenopathy usually appears as a consequence of infection in the nasopharynx. The spleen is usually palpable but rarely more than 2 to 3 finger breadths below the costal margin. Purpuric and ecchymotic lesions of the skin and mucous membranes are common. As the number of mature granulocytes decreases in the peripheral blood, the throat may resemble the angina of agranulocytosis with ulceration and necrotic areas resulting in a very foul odor to the breath. Invasion of the gums by leukemic infiltration is most commonly seen in the monocytic type but occurs in other types as well (Fig. 89). The fundi show the changes mentioned above with greater severity. In the later stages of the disease almost the entire metabolism of the body seems to be given over to the leukemic process with increased metabolic rate, fever, rapid breathing, tachycardia, and prostration.

The hematocrit in leukemia will characteristically show a reduced red cell mass and a greatly increased buffy coat. However, in some cases leukemia will be associated with a normal or even reduced white count, in which case the diagnosis must be made by recognition of abnormal white cells in the smear.

LYMPHOMAS

The lymphomas comprise a group of diseases involving lymphatic tissue and having the characteristics of a malignant growth. The identification of the exact type of lymphoma is based on histological criteria. Their course usually parallels that of the leukemias previously described, and often the only differential point between a lymphoma and a lymphatic leukemia depends on the presence or absence of malignant cells in the blood and changes in the white cell count.

The most characteristic manifestation is enlargement of the lymph nodes (Fig. 147). In the cervical area the nodes may be noted by the patient and cause him to seek medical advice. Enlarged nodes in the mediastinum may produce pulmonary symptoms, hoarseness from recurrent laryngeal nerve involvement, Horner's syndrome from cervical sympathetic chain involvement or a chylous pleural effusion from thoracic duct involvement.

the cervical area. These nodes are almost never tender Early in the course of the disease the nodes are discrete and freely movable, tending to become matted together and fixed to adjacent tissues only late in the disease. They have a firm "rubbery" or at times cartilaginous consistency seldom confused with the stony hardness of carcinoma.

Lymphomas may arise in lymph tissue outside the lymph nodes Such lesions arising in the tonsils or nasopharynx are not uncommon and result in one of the most distressing forms of the disease Bleeding is often the first symptom of such lesions in the intestinal tract, though obstructive symptoms sometimes occur. Pathological fracture may be the first indication of bone involvement. Invasion of nerves may produce sensory or motor changes.

Lymphomas and leukemias involving the skin are often confused with primary diseases of the skin. These tumors often appear first as small erythematous infiltrated areas progressing to nodule formation and finally ulceration (Fig 18). The skin lesions may be present for months or years

before the systemic manifestations are apparent. Itching of an intractable nature is often encountered, either with or without skin involvement.

As the disease approaches its terminal phase, a rather characteristic picture is produced. The spleen and liver are often palpable. Weight loss and cachexia become prominent. Anemia appears due to bone marrow invasion, "toxic" inhibition, or the x-ray therapy. Lymph node enlargement may produce severe symptoms of pressure and invasion of adjacent structures Either as a result of the disease or of the concomitant x-ray therapy platelets and granulocytes are depressed with resultant bleeding and infection. An intercurrent infection is usually the cause of death.

INFECTIOUS MONONUCLEOSIS

Infectious mononucleosis is a disease of unknown etiology and characterized by fever, lymphadenopathy, and a sore throat The fact that it is a benign disease is of great importance in view of the ease with which it may be confused with leukemia. The manifestations of this disease are protean and any one or several of the characteristic features may be missing. The lymph node enlargement is almost always most noticeable in the cervical area. Fever is usually of moderate degree, though it may be high or absent. The spleen is palpable in about half the cases. In about 10 per cent the liver is palpable and jaundice is present. A skin rash of an erythematous macular or maculo-papular nature also occurs. Headache is a common symptom and occasionally signs of meningitis are present. Of importance in differentiating this benign condition from leukemia is the positive heterophile test, characteristic appearance of the lymphocytes on smear, and normal platelets and red blood cells

RADIATION EFFECTS

Of the many pathological effects produced by ionizing radiation, the most dramatic and devastating are those concerning the blood cells, and consequently a discussion of such effects will be given here. This is particularly pertinent in view of the recent rapid increases in the potential sources of exposure to ionizing radiation.

With a single intense exposure of low energy radiation with little penetration, the effect is confined to the skin and superficial layers and resembles any other thermal burn. When the radiation is penetrating, exposure is usually followed in a few hours by nausea and vomiting. This in turn is followed by a latent period measured in days. The greater the dose received, the shorter the latent period and the more severe the subsequent symptoms. These symptoms consist of recurrent nausea and vomiting, diarrhea, bleeding, epilation and, most important, the symptoms of agranulocytosis as previously described. The blood changes (Fig 600) consist of an absolute lymphopenia appearing in twenty-four to seventy-two hours and often accompanied by a moderate leukocytosis. Subsequently the granulocytes decrease, the eventual level depending on the dose. A slight, sustained increase in granulocytes should appear within three weeks if the dose is not lethal. The changes in the platelets are not so predictable but certainly a bleeding tendency is one of the potentially lethal manifestations of exposure to ionizing radiation. Because of the relatively long life of the red cells, anemia does not appear in the early and critical stages of the syndrome except as a secondary complication of the bleeding tendency.

Chronic exposure to small quantities of ionizing radiation produce insidious and progressive changes, many of which remain to be described. At present 0.1 r per day is considered to be the maximum exposure tolerable. Again the effect produced must be referred to the degree of penetration. Handling of radioactive materials with the fingers may produce patches of atrophy, loss of fingerprints, and loss of sensation of the fingertips. A common manifestation is brittleness and increased longitudinal ridging of the fingernails. Atrophic lesions of the skin may be followed by pigmentation, ulceration and carcinoma, the latter appearing often after a latent period of many years. Epilation of hair parts may occur. Cataracts may appear if the eyes are exposed to excessive radiation. The effects of chronic exposure to ionizing radiation on the blood are quite variable, as indicated by the reports describing leukocytosis, lymphocytosis, leukemoid reactions, leukemias, erythrocytosis, reticulocytosis, leukopenia, thrombocytopenic purpura and aplastic anemia. The clinical picture of these various reactions has been described in the other sections It is important to note that these effects may not become clinically apparent until irreversible changes have occurred.

Hemorrhagic Diseases

ALLERGIC AND VASCULAR PURPURA

Vascular purpuras represent the most common type of bleeding tendency. There are numerous causes of this type of purpura, including *vitamin C deficiency, nephritis, various toxic drugs and serum sickness.* The defect appears to be due to increased blood vessel fragility, as the coagulation mechanism is normal.

Allergic purpuras as a rule do not have an associated thrombocytopenia. The hemorrhagic lesions are associated with other signs of an allergic reaction such as erythema and effusions of plasma resulting in wheals or vesicles. The fundamental lesion seems to be an increased capillary permeability allowing the passage of serum and blood cells into the tissues. The lesions tend to occur in crops and are variable and recurrent. *Henoch's purpura* is a type of allergic purpura in which the lesions occur in the intestinal wall. The resulting symptoms include colic, tenderness without spasm, tenesmus, constipation, and vomiting Intussusception may be initiated by the localized hemorrhage in the gut wall. Fever is common, but moderate. *Schönlein's purpura* is also an allergic purpura with the chief manifestations from lesions about the joints. The lower extremities are most frequently involved, with pain, tenderness and swelling of the involved joints and with increased capillary fragility or purpuric lesions of the skin True hemarthroses do not occur.

THROMBOCYTOPENIC PURPURA

Thrombocytopenia, or decrease in platelets in the circulating blood, may be caused by many conditions such as physical or chemical agents, infections, and primary blood disease. One must make a careful search for a history of causative factors, particularly drugs, on encountering a case of purpura. Idiopathic thrombocytopenic purpura is a disease of unknown cause occurring usually before the third decade, but occasionally seen in older age groups. The first complaint may be with reference to the petechial

lesions in the skin, nosebleeds, bleeding from the gastro-intestinal or urinary tract, menorrhagia, or cerebral hemorrhage. Often a previous history of a tendency to bruise easily can be obtained. In children the disease tends to be mild, but in older age groups there is a tendency for recurrence, and a history of a previous episode may be obtained. Physical examination shows primarily the petechiae with possible ecchymoses, mucous membrane lesions, and bleeding from the gums. The spleen is palpable in only one third of the cases and is almost never of great size. There is no lymphadenopathy, and signs of anemia are present only if bleeding has been sufficient to cause it. Fever of moderate degree is common. Before a thrombocytopenic purpura may be called idiopathic, the various known causes must be excluded. Chemical agents producing thrombocytopenia most commonly are organic arsenicals, gold salts, sedormid, benzene, sulfonamides, and salicylates, though many others have been indicated. Purpura associated with leukemia, aplastic anemia, myelophthisic anemia, etc., will have signs of the primary disease as described elsewhere. A greatly enlarged spleen from any cause (hypersplenism) may produce a thrombocytopenia and purpura.

HEREDITARY HEMORRHAGIC DISEASES

Hemophilia is an hereditary disease occurring only in males and characterized by severe and prolonged bleeding after trauma. Recurrent bleeding into the joints usually leads to deformity and eventual ankylosis. Prolonged hematuria occurs, and fatal hemorrhage may ensue after surgical procedures. Congenital *hypoprothrombinemia* and *fibrinogenopenia* are less frequently encountered but are also characterized by bleeding after trauma and by ecchymoses. Hypoprothrombinemia due to dicumarol or liver disease with resultant hemorrhage is more frequently seen. In von Willebrand's disease one finds a nonthrombocytopenic condition with purpura and other bleeding manifestations, and characterized by a strong family history of bleeding in both sexes.

DIAGNOSIS OF HEMORRHAGIC DISEASES

The history and physical examination are of limited value in determining the exact type of bleeding tendency However, one should keep in mind the following points. (1) a history of drug ingestion or exposure to a toxic physical or chemical agent, (2) a history of previous episodes of bleeding, and (3) a history of a similar illness in the family. The appearance of the hemorrhagic lesions gives a clue to the etiology. Small petechiae are more likely to occur as a result of platelet deficiency or vascular injury (Fig. 596), while, as a rule, the larger hemorrhages indicate a defect in the coagulation mechanism (Fig. 597). Several methods are available to bring out a latent tendency to form petechiae. Because of the crudeness and variability of these methods it is important for the student to select a particular method and use it in a standard fashion. The tourniquet test is probably the most widely employed method. A blood pressure cuff is applied to the upper arm, inflated to a pressure of 90 millimeters of mercury, and allowed to remain for ten minutes, the observer being prepared to remove it if large numbers of petechiae begin to appear. The number of petechiae appearing in 1 square inch located four inches below the fold of the elbow is counted. If more than twenty appear the test is considered positive. The entire arm distal to the tourniquet should be inspected for petechiae, however, since

occasionally they occur only in small areas. The determination of bleeding time is done by puncturing the ear lobe with a sharp pointed scalpel blade and then touching the bleeding point with filter paper every thirty seconds until bleeding has stopped. The bleeding time is normally one to four minutes. A crude test of clotting time is done by placing 2 cc. of blood in each of two Wassermann tubes, tilting the first tube gently until the blood clots and then tilting the second tube until it clots, the normal time for the second tube to clot being six to twelve minutes. In vascular purpura there is no abnormality in blood coagulation. The bleeding time and clotting time are within normal limits and the tourniquet test may or may not be normal. In thrombocytopenic purpura, the clotting time is normal but the bleeding time and tourniquet test are abnormal and platelets are decreased or absent on the smear. A prolonged clotting time is the only abnormality in hemophilia. With hypoprothrombinemia as produced by dicumarol, there is usually no abnormality in any of these tests.

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XXII

THE CHILD

The pediatric period is usually considered to cover the period from birth to fourteen years of age. In the opinion of many pediatricians it should extend through adolescence or for the first sixteen years of life. Since infancy and childhood are characterized by growth it is necessary in any discussion of physical diagnosis to include pertinent data on growth and development The following discussion thus includes much material on growth and development plus considerable material on the examination of the infant and young child. Since examination of the older child varies little from that of the adult little space is devoted to this subject.

The pediatric incidence of diseases varies greatly from the adult incidence, therefore the common diseases in this age group are recorded when indicated.

Approach to Examination. The approach to the examination of the average child varies with age. Under six months of age only gentleness is necessary to prevent alarm. After this age the infant's reaction will vary with his experiences in previous examinations. It usually is well to record the history with the small child in the room, while apparently paying him little attention. In this way he becomes accustomed to the examiner and the examiner in turn may get valuable information from the activities and reactions of the child. Under four years of age it is well to examine the abdomen and to auscultate the heart before the child has an opportunity to cry, as the remainder of the examination can be done with fair accuracy, even though the child is crying. Under two years of age it is useless to try to quiet the child by firmness or diversion, once he becomes excited, as these efforts usually result in greater excitement.

The child is much more likely to cooperate when examined in the familiar surroundings of the home and here one often can get a better picture of the individual and his environment. Most children will allow an examination if they are properly approached and have not been frightened by other physicians, the parent who threatens the child with a visit to the physician invites fear and rebellion. The older child may be put at ease by talking to him about his daily activities, school, and the like.

In order to gain the child's confidence, the physician should always tell him when a procedure, e g , venepuncture, is likely to be painful.

THE NEWBORN INFANT

The newborn (neonatal) period, extending from birth to two weeks of age, is one of rapid readjustment. Emerging from a parasitic, marine existence the infant is thrust into an environment in which he must adjust his own temperature regardless of that of his surroundings, must use his respiratory system efficiently and at once in order to insure his oxygen

supply, and must ingest and digest his food in sufficient quantities for his caloric needs in order to survive. He has just passed through a period of potential and actual trauma which makes the task of adjustment more difficult.

The newborn arrives in the world as a distinct individual. He may be said to be composite of the interplay of genes inherited from both parents plus the intra-uterine environment to which he has been subjected. These factors necessarily vary with every child, and deviation in form, size, emotional reactions and adjustment to extra-uterine life vary considerably with each infant.

Examination

The newborn infant is examined mainly to discover birth injuries, congenital abnormalities, and certain diseases which occur during this period A careful evaluation must include a history of the mother's pregnancy as well as a knowledge of the length and character of labor

Common Conditions in the Newborn Period

Acidosis	Intracranial hemorrhage
Anemia	Malformations
Atelectasis	Nerve injuries (brachial and facial palsy)
Cephalhematoma	Pneumonia
Dehydration, fever	Pneumothorax
Epidemic diarrhea	Pyelonephritis
Erythroblastosis fetalis	Septicemia
Fractures (clavicle, long bones, base of skull)	Sternocleidomastoid muscle injury
Hemorrhagic disease (Vitamin K deficiency)	Syphilis
Icterus neonatorum	Tetany of newborn
Impetigo	Thrush

Weight. The infant is considered full-term at birth if he weighs 5½ pounds (2500 gm.). For purposes of classification all infants below this weight are considered premature, whatever the length of gestation Many infants who weigh more than 2500 gm. are less vigorous than some of those below this weight level and these infants are termed immature. A body length of 19 inches (47.5 cm) is usually considered the lower limit of maturity, though the weight is the more commonly used criterion. The infant is born edematous due to the water medium surrounding him in utero He then loses 5 to 8 per cent of his birth weight during the first five days of life, gradually regaining this weight by the tenth to fourteenth day.

Skin. *The skin of the infant at birth is purplish red in color and is covered* with a cheesy material, vernix caseosa, which apparently has antiseptic qualities. Skin infections are uncommon if the vernix caseosa is left intact except in the fissures and the infant is not given a bath for the first nine days The use of bland antiseptic oil on the skin during the neonatal period aids in preventing desquamation and excoriation of the skin as well as impetigo Fine capillary angiomas are common at the nape of the neck, in the frontal area just above the nose, on the eyelids and upper lip. These fade and after one year are visible only when the skin is flushed

Hair. The infant's scalp in pigmented individuals often is covered with a heavy growth of hair while blondes may have only a fine down. The hair usually is replaced by hair of coarser texture and more or less pigmented. The body especially the face, shoulders and back is covered with "lanugo," a fine downy hair.

Nails. The nails of the full-term infant usually are long tl
thin and brittle.

Head. The head at birth is large as compared to other parts (
the average circumference in the full-term infant being 35 cm. (1.
The cranium has a capacity of about 400 cc. as compared to 14(
adult. In vertex presentations there is marked molding of the
pointing in the parieto-occipital area which gradually disapp
two weeks when the occipital, parietal and frontal eminences be
prominent. Usually there is marked over-riding of the cranial b
also is corrected during the first month of life. Six fontanels a
The anterior is the largest being about 1½ inches by ½ inch (3
and diamond-shaped. The posterior fontanel will admit only th
finger, the two posterolateral ones are even smaller, while the a
ones can be palpated with difficulty. The margins of the cra
forming the suture lines are quite soft and easily compressibl
and none of the bones forming the vault of the cranium have fus
inspection for bruises and masses must be done; gentle palpat
eliminate defects in the cranial bones, masses due to trauma (cap
neum, cephalhematoma) and depressed fractures of the skull.

Face. The face at birth is relatively small; it comprises one
bulk of the cranium as compared to one half in the adult. Its s
due mainly to the smallness of the jaws with their unerupted te
lack of development of the paranasal sinuses. Not infrequently f
paralysis occurs, especially following forceps delivery, while e
about the eyelids are not uncommon after difficult deliveries.

Eyes. The newborn infant's eyes are quite sensitive to light,
attempt at examination causes him to close his eyes and to resis
tion. Ophthalmia neonatorum due to the gonococcus always mu
sidered if there is purulent discharge during the first weeks o
eyelids during the first few days of life are somewhat edematous
is often a slight "chemical" conjunctivitis resulting from inst
silver nitrate solution, which may be confused with gonococcal o
There may be ecchymoses of the conjunctivas resulting from lab
application, and the like.

Iris The iris usually is blue at birth In dark-complexioned
may acquire pigment and become brown between one and twelve
age. It is seldom the seat of abnormality. Both pupils are equal :
react normally to light.

At birth there is lack of balance and coordination of the e
muscles, so that the infant does not converge, or accommodat
eyes may at times show convergent or divergent squint. Howe
is seldom permanent deviation in one direction. Coordination
acquired during the first three months of life, though some infant
coordinate constantly before one year of age. Examination of
ocular movements is difficult; one can only observe the involunt
ments of the eye.

Sclera. The sclera at birth has a bluish white tint as it is thi
choroid shows through it. It may normally be icteric during *the fi*
of life.

Lacrimal Gland The infant may not shed *tears for the first tv*

Lens. The lens is usually clear and colorless but occasionally is the seat of congenital cataract which makes careful examination necessary

Vision. With regard to vision, one may state that at birth the child probably perceives only light and darkness, images being recognized only [illegible] tion (5 per cent euphthalmine is recommended as a cycloplegic in order to prevent reactions to atropine).

Ears. The external ear seldom is abnormal in the newborn. It has the general configuration of that of the adult and may vary in shape within normal limits. The auditory canal is quite small and usually its walls are covered in the outer portion with fine, long hairs, making examination of the ear drum difficult. The canal runs more obliquely downward and forward than in the adult. The drum also is more oblique in relation to the canal with the lower anterior part more distant from the external ear. As infections of the middle ear seldom occur during the neonatal period an extensive examination need not be done routinely. (See examination of ears in infancy, p 993.)

Nose. The nose is small and the air passages quite narrow. The septum usually is in the midline and perforation or malformation is rare. Early, purulent inflammation rarely occurs, a discharge at this time, especially if persistent and blood tinged, is likely to be syphilitic.

The sense of smell develops later than the other senses, so that detection of fine differences in odors is not acquired until later childhood The maxillary antra and ethmoid sinuses are developed at birth, while the sphenoid sinuses are rudimentary. (See also Chapter VI, p. 182.) The frontal sinuses are small but usually are demonstrable by x-ray at the age of six to twelve months Sinus infection is rare during the newborn period The nose should be inspected for discharge, abnormalities of the septum and obstruction to breathing.

Mouth. In the newborn infant, the mouth is the seat of three common abnormalities, harelip, cleft palate and tongue-tie or shortening of the frenum (Fig. 84, Chapter V) Inflammation other than thrush (mycotic stomatitis) is rare. The tongue is clean, moist, pink in color, and an attempt at examination usually provokes the sucking reflex The teeth are not erupted, though occasionally an infant is born with one or two teeth partially erupted. The gums are a salmon pink color, lighter than the lips, firm on pressure and do not bleed easily The palate differs little from that of the adult; the soft palate elevates normally on gagging the infant

The sense of taste develops rapidly, so that at two days of age an infant will refuse liquids of disagreeable taste.

Throat. The tonsils are small and pink The pharynx is a healthy pink and seldom can lymphoid tissue be seen Considerable pressure on the tongue is necessary to examine the soft palate and pharynx It is best done by resting the body of the infant on the left forearm while grasping the back of the head with the left hand. The tongue depressor in the right hand may now be inserted exposing the posterior pharynx. In this way one may move the infant to get the best light.

Larynx. Examination of the larynx is difficult in the newborn and seldom is necessary. Mucus sometimes accumulates in the nasopharynx causing

difficulty in breathing and should be aspirated with a soft rubber bulb syringe. The cry of the young infant is characteristically low-pitched and in a monotone. He normally cries several minutes three to four times daily, usually before feedings.

Neck. The neck appears short due to the relatively large size of the head, the amount of subcutaneous fat, and the height of the clavicles. Forcible bending of the neck may result in embarrassment of respiration. The skin in this area is quite thin, delicate and moist and often becomes slightly excoriated in the folds. Special attention should be given the sternocleidomastoid muscles (hematoma), the presence or absence of lateral or midline neck sinuses (branchial cyst) and palpable neck masses (hygroma). Enlargement of the cervical lymph nodes at birth is abnormal.

Chest. The chest of the newborn infant is smaller than the head, being about 33.5 cm. (13½ inches) in circumference. It has been described as "a truncated cone flaring widely at the bottom but with slight anteroposterior flattening." The clavicular fossae are filled with subcutaneous fat and are not prominent, though they vary with the nutrition of the individual infant. In the normally expanded chest of a newborn infant the ribs are almost at right angles to the spine. Respiration is mainly diaphragmatic (abdominal). The rate varies from 35 to 45 per minute and is regular only during sleep. The examiner should look for congenital atelectasis, minor degrees of which seldom can be determined clinically. Percussion should be light Immediate percussion often is very valuable. Auscultation is most informative. The breath sounds are rather feeble early in the newborn period though the pitch is rather high and expiration can be heard almost as well as inspiration. The infant must be made to cry in order to determine the presence or absence of rales.

With the first respirations the alveoli begin to expand, especially at the anterior borders and apices of the lungs Full expansion as determined by x-ray studies is usually complete at one week. Microscopic studies have revealed that expansion may not be complete for several weeks Pneumonic processes are extremely difficult to diagnose from physical signs alone and x-ray diagnosis should be resorted to in unexplained fevers in newborn infants

Heart. The heart rate is 130 to 140 per minute and the sounds are regular and strong The outline is difficult or impossible to determine by percussion and the point of maximal impulse seldom can be palpated with accuracy. One should determine the location of the heart sounds and the absence or presence of murmurs that may be congenital. Functional murmurs at the base may be present in the neonatal period, so that without objective signs one must hesitate to diagnose congenital heart disease simply on the presence of a murmur, unless it is of unusual intensity. X-ray and fluoroscopic studies of the heart are indicated when a suspicious murmur is found. Blood pressure cannot be accurately determined clinically at this period, though

wound. Only gross enlargements of the liver, spleen or kidneys, and the presence of large masses may be noted. The spleen normally may be felt at the costal margin and the liver may extend 2 to 3 cm. (½ to 1 inch) below this level.

Umbilical Cord. The umbilical cord normally separates about the fifth day, and by the age of ten to fourteen days the umbilical wound usually is healed. Small bits of granulation tissue, unless cauterized with silver nitrate, may prevent complete healing for a considerable time. Umbilical hernia is more common in Negro infants.

Genitalia. The genitalia should be inspected for evidence of abnormality. In the male, phimosis is the rule and forcible retraction of the foreskin or circumcision is necessary. Retraction can best be accomplished by gentle daily attempts at retraction of the foreskin The testicles often are found near the external inguinal rings, as the cremasteric muscles are quite active. Congenital hydrocele is common especially on the right side. Hypospadias or epispadias may occur. Erectile tissue is present and erection often occurs immediately before the infant voids In the female a mucoid, occasionally blood-tinged discharge may normally be present during the first week of life In this connection, enlargement of the breasts of newly born infants is common during the first month of life, apparently due to hormonal substance derived from the mother.

Anal Region. The anal region should be inspected for fissures, fistulas and stenosis or atresia Digital examination should be avoided if possible. Anovaginal fistulas are rare, unless accompanied by rectal stenosis.

Extremities. The extremities are short as compared to the length of the body. The muscular development is poor but is obscured by subcutaneous fat and edema which give the extremities a rounded appearance Congenital abnormalities in the upper extremities are rare, but injuries to the nerves (brachial plexus) or to the bones (fracture of the humerus) are common

The lower extremities are covered with a heavy layer of subcutaneous fat Congenital abnormalities (e. g , clubfeet, congenital dislocation of the hips) occur in one per 1000 births In breech presentations, injuries are frequent (fracture of the femur).

Neurological Examination. Neurological examination of the newly born is concerned mainly with objective signs, or motor reactions due to injury at birth or to malformation Motor activity during this period is almost entirely reflex with little evidence of coordination. Isolated paralyses, such as facial paralysis, or flaccidity of one or more extremities are of importance. The biceps, triceps, patella and Achilles tendon reflexes tend to be hyperactive; the Babinski normally is positive. Of special value is the *Moro embrace reflex* which is elicited by sudden removal of support of the baby, or startling by a loud noise The arms are suddenly thrown outward following which they are brought together in a jerky manner. The fingers at first are fanned, then the hands are closed. The legs usually flex but may extend Any asymmetry of response may be due to birth trauma of the nervous or skeletal systems. In the *tonic neck reflex* the arm is

most infants, though brain edema may result in its temporary absence in the first 24 hours. *Babinski's sign* often is positive in the newborn infant and may remain so until the infant walks alone. *Chvostek's sign* often is present in the normal newborn. The deep reflexes are present, symmetrical and easy to elicit Absence of the *abdominal reflexes* is not significant. Sensory tests are of little value. Gross loss of pain sense may be determined by a series of light pricks with a pin

THE INFANT AND CHILD

Temperature. The temperature can be taken only by means of a thermometer; estimation by the degree of warmth of the skin is not a reliable method. Rectal temperatures should be taken in children under the age of six years, and in those acutely ill. The normal rectal temperature in infancy and childhood is 99.5° F. (37.5° C.) and the normal mouth temperature 98.6° F. (37° C.). It is subject to slight variations early in life, being lowered on exposure to cold and raised (less than 1° F.) by excitement, crying or excessive fatigue.

Pulse. The pulse rate is quite rapid in early life and decreases in rate as the child grows. The average pulse rate per minute is as follows:

Infants	120–140
First Year	110
Second Year	100
Fifth to Eighth Year	90

The pulse rhythm is regular from birth, though sinus arrhythmia is common in childhood causing a "regular irregularity" in the pulse. The rhythm and rate are subject to great variations on excitement or crying. The radial arteries are easily compressible in childhood, as arteriosclerosis is extremely rare.

Respiration. Respiration is irregular at birth and may be irregular throughout infancy when the infant is excited. The respiration is abdominal in type, becoming thoracic in later childhood. Respiration (rate per minute) is as follows:

Newly born	35–45
First to second month	24–36
Second to sixth month	20–32
First to second year	20–25
Second to sixth year	20–23
Sixth to twelfth year	18–20

Height and Weight. In early life the height bears a definite relation to weight so that one always must consider both in attempting to judge a child's nutritional state. The factor of body build due to heredity also must be considered. In order to accurately determine the average weight for height and body type, it is necessary to consult tables which include the width of the individual, as determined by the distance between the crests of the ilium (interiliac or bicristal diameter). Prior and Stolz have compiled such tables for children from one to sixteen years. The state of nutrition can be rather accurately estimated when one compares the height and weight for age and roughly determines the body type by determining the interiliac diameter. (See also Figs *586, 587, Chapter XIX.*)

The Head. Before the age of seven years, particularly during the first two years, the head grows rapidly. From then until the onset of puberty growth is much slower. The sutures are united by six to nine months of age The posterior fontanel closes by two months and the anterior fontanel by eighteen months of age. The head may vary considerably in shape, being long and thin or short and rounded. Flattening occurs in the occipital region if the young infant is allowed to lie continuously on his back. The head must be carefully inspected for symmetry and shape and the measurements taken; gentle but firm palpation determines abnormal masses, delayed

or early closure of the sutures and fontanels and softening (craniotabes, found most often in the parieto-occipital areas) of the cranial bones.

The Face. The face increases relatively in size from the second to the fourth year when it assumes approximately the normal adult proportion to the cranium. The normal shape may vary from the narrow type with narrow nose, high orbits, narrow long palate and a delicate lower jaw, to the broad flat type with broad nose, low orbits, a square jaw and wide nasal apertures. While no face is absolutely symmetrical, easily discernible variations in symmetry are considered abnormal. Much may be learned as to the mental status of certain individuals by inspection of the facies (mental deficiency, mongolism, cretinism; see also Chapter V, p. 122).

The Eyes. The normal eye of a new born infant differs from that of the adult in size, the color of the irises (dark slate-blue), the size of the pupil (miotic) and in the muscular incoordination. The lacrimal gland begins to secrete tears at two months Vision is deficient in infancy (lack of complete myelinization of the optic nerve) but by three months the child should be able to notice and follow a light with only moderate incoordination of the ocular muscles. The extraocular movements are tested in the usual manner, using a light to attract the attention of the young infant. At six months he should be able to recognize familiar persons. At three years the standard illiterate test cards are applicable.

The position and size of the eyeball are noted, as well as the size of the palpebral apertures and the condition of the lashes.

Congestion, secretion and granulations of the conjunctiva must be looked for (purulent secretion in infancy often is due to stenotic canaliculi at birth with subsequent stagnation of tears)

The *cornea* is inspected for ulcers, scars, nebulae, keratitis (tuberculosis, syphilis, allergy, dietary deficiency, trauma) and the corneal reflex is tested by touching the cornea (not the lashes) with a fine wisp of cotton.

The *sclera* is inspected for congestion and blue (fragilitas ossium) or yellow discoloration.

The *lens* is studied for opacities (after dilating the pupil with 5 per cent euphthalmine) using a plus 12 lens and oblique illumination Reduce the plus sphere of ophthalmoscope and gradually study the optic disk for elevation, papillitis or papilledema, blurring of edges, size and shape of physiological cup and color atrophy. Inspect the macula for a cherry red spot and the peripheral fundus for pigmentation, fulness of veins, hemorrhage, color and tortuosity of arteries and arteriovenous compression.

The Ears. In the young infant the oblique position of the ear drum in relation to the canal and small size of the canal make examination difficult. As the skull grows the canal slopes less sharply and the tympanic membrane is less obliquely situated. Fine hairs lining the outer part of the canal may obscure the drum. A cotton applicator, with a light coating of vaseline, rotated in the canal will cause these to adhere to the wall. Soft wax must be removed with a small round edge ear curette and hard wax softened by irrigation with hydrogen peroxide or tap water Younger patients must be restrained by using a sheet or small blanket as a wrap.*

it in place. Pull the left side of the blanket across the baby's body, tuck it well under his back at the right side, and pin with two large safety pins

Adequate examination of the auditory canal and ear drum can only be done with an electrical otoscope (holding the auricle directly backward). Good illumination is essential. Special attention must be paid to the canal wall, the membrana flaccida, the long and short processes of the malleus, the cone of light, and possibly bulging or changes in texture and color of the ear drum (Plate VIII, p. 196). Accurate testing of hearing is difficult under four years of age, though an infant of six months will turn his head toward the ticking of a loud watch. Later, rough tests may be done by determining the distance from the ear at which a watch may be heard. Audiometer readings are necessary after six years of age if accuracy is desired. (Common ear conditions: otitis media, mastoiditis, furunculosis of external canal, congenital nerve deafness.)

The Nose. The general configuration of the nose of the infant is similar to that of the adult. The size and shape must be noted, as well as evidence of inflammation or excoriation of the upper lip, due to nasal discharge. One must ascertain whether the septum is intact; the broad, flat nose of the Negro often is deceptive. Nasal obstruction may be determined by occluding one nostril, causing the patient to breathe through the other with the mouth closed. The anterior nares are best examined with a nasal speculum and a light. The large speculum of an electrical otoscope is adequate and convenient. Care must be taken not to press the instrument against the sensitive nasal septum. The mucous membrane of turbinated bones should be examined for inflammatory changes, and the meati for purulent discharge. In the young subject the inferior turbinated bone is quite small.

The *septum*, which usually is in the midline before the sixth year of life, should be inspected for inflammation, ulceration or deviation.

The *adenoids* and *posterior nares* are best examined by means of a nasopharyngoscope in practised hands. Lack of cooperation makes the use of the pharyngeal mirror difficult in young children. Adenoid enlargement is presumed if the infant has recurrent otitis media or is a consistent "mouth breather." Examination of the paranasal sinuses should include careful external inspection for inflammation, palpation for edema or tenderness, and inspection of the meati for discharge Transillumination of the maxillary sinuses (Plate VII, p. 179) is deceptive due to the presence of unerupted teeth; the frontals may be easily transilluminated. X-ray films of the sinuses are valuable diagnostic aids (Figs. 122 and 123, Chapter VI). (Common conditions: common cold, sinusitis, adenoid hypertrophy, foreign body in nose, epistaxis)

The Mouth. The condition of the lips must be noted. They normally are rose-red, but vary greatly in different individuals. One must look for scarring or ulcerations. Careful inspection with a good light, preferably daylight, must be given the buccal mucous membranes, gums and teeth, the tongue and the hard palate before alarming the patient with the more formidable throat examination. The uncooperative younger patient must be restrained by an attendant.

The *tongue* normally is clean, red and moist; the frenum is inspected for

tant and often is neglected. There are twenty deciduous teeth and the

average time of appearance are given in the chart in Chapter V, p. 127. At one year a child should have six teeth, at eighteen months twelve, at two years sixteen, and at two and one-half years, twenty teeth.

In the permanent teeth the eight bicuspids replace the eight molars of the first set and the molars appear back of these, room being made by the growth of the jaw. They appear as indicated in the table on p. 127.

The *gums* normally are a healthy salmon-pink, rather firm, and bleed easily when injured. They may become quite red and edematous as teething occurs. (Lancing to permit eruption of a tooth should never be resorted to.) The palate has the same configuration as in the adult; the soft palate should elevate normally. Cleft palate is a common abnormality. Several small, white papules may normally be seen along the median raphe in many infants and children.

The Throat. The throat examination must be done rapidly but with accuracy. An experienced observer recognizes the normal throat at a glance, but otherwise a longer, careful inspection is necessary. (See also Chapter VI, p. 184.) The size and color of the tonsils must be noted, as well as the pharynx. *Inflammatory changes of the anterior faucial pillars (over the* tonsils) must be looked for. The patient must be gagged to determine the presence of a posterior nasal discharge behind the uvula When there is respiratory difficulty in infancy, retropharyngeal abscess is ruled out by palpation of the posterior pharyngeal wall If there is chronic nasal discharge *or obstruction to nasal breathing (mouth breathing) the adenoids may be* palpated by the index finger, after a mouth gag is in place This can be done between six months of age and three years of age, though it is rather brutal. The adenoid masses impart to the finger the sensation of feeling a few irregular masses of fat. In older children the use of the nasopharyngoscope is the more accurate method

Examination of the *vocal cords* can seldom be done with the mirror before the age of six years. When indicated, a laryngoscope may be used to determine inflammatory or paralytic changes in the larynx. This is a relatively simple procedure in practised hands

Common Conditions of Mouth and Throat. (See illustrations in Chapter V.) These are. harelip and cleft palate, tongue-tie, geographic tongue, stomatitis (infectious diseases, aphthous, Vincent's, mycotic), dental caries, pyorrhea, common cold, pharyngitis and tonsillitis, retropharyngeal and peritonsillar abscess.

The Neck. The short neck of the infant loses much of its fat by one year and seems relatively longer. Stiffness, pain on motion, or hyperextension of the neck are noted (See also Chapter VII, p 215) Evidences of lymph node enlargement, sinus formation, enlarged thyroid gland or venous pulsation should be carefully searched for. Slight enlargement of the lymph nodes at the angle of the jaw and along the cervical chains is not unusual after one year of age.

Because of the frequent enlargement of the lymph nodes about the head and neck, knowledge of their approximate drainage areas is essential. The preauricular nodes receive drainage from the anterior half of the scalp, the surrounding skin and the upper pharynx. The *submandibular* nodes drain the skin of the face and neck, the buccal cavity, the gums of the lower jaw, the anterior part of the tongue and the tonsils. The *superficial* cervical nodes drain the skin of the face and neck, the pharynx and the external

ear. The *upper deep cervical nodes* drain the buccal cavity, posterior part of the tongue, tonsils, palate, and lower pharynx. The *suprahyoid nodes* drain the anterior part of the tongue, and the retropharyngeal nodes drain the pharynx.

Common causes of lymph node enlargement: acute infection, tuberculosis, Hodgkin's disease, malignant neoplasm, leukemia.

The Chest. The chest examination must be done with the patient stripped and in a good light. *Inspection* is of great importance and often is neglected. In early infancy the chest may be symmetrical, with equal measurements, but as the child grows the right side may be better developed than the left. In infancy the ribs are more horizontal, the heart larger, the lungs smaller and the thymus relatively larger than in the older child. The clavicles are higher and covered with adipose tissue in infancy. Before the age of six years, breathing is mainly of the abdominal type.

One must note especially the size (measurements) and development, the shape and symmetry, and the degree of expansion of the chest; also the type and rate of breathing, size and motion of the subcostal angle (it should be a right angle without flaring of the costal margins), and the ease of inspiration. Retraction of the intercostal spaces is especially important as is the presence of Harrison's groove (a transverse furrow corresponding to the attachment of the diaphragm), enlarged costochondral junctions (rachitic rosary) and prominence or depression of the sternum.

Palpation. Vocal fremitus is elicited by laying the ulnar surfaces of the hand or fingers upon symmetrical areas of the chest as the child repeats one-one-one in a clear voice; the vibration is faint in infancy and early childhood due to lack of a resonant voice. It is more marked over the right upper lobe and posteriorly between the scapulas. Expansion can best be determined by placing the hands on the chest and inspecting the relative motion of the two sides

Percussion To be of value, percussion must be very light; often, gentle tapping with one finger reveals minor changes. The sense of resistance imparted to the finger is of as much value as the note which is heard In early life the percussion note is higher pitched than in adults The child should be in a sitting or standing position if possible but never on one side, as the flexible thorax is easily compressed thus yielding a less resonant note on the dependent side. The posterior chest is best examined while the infant is held in the nurse's arms. In infancy the percussion note is resonant or slightly hyperresonant on the right side to the fourth rib anteriorly and to the eighth rib posteriorly. Below these levels the note gradually becomes dull due to the liver. On the left side "gastric tympany" may affect the normal note as high as the sixth rib. The note may be slightly dull below the inner third of the clavicle on the left side, and it shades into the cardiac dulness This slightly dull area may be due to poor expansion of the left apex over the great vessels, or in part to the left lobe of the thymus gland. The *thymus* cannot be percussed with accuracy even when it is enlarged. Lateral x-ray plates are of greater value than anteroposterior ones in ruling out symptomatic thymus enlargement.

Auscultation. In infants it is well to listen both when the patient is quiet and also when he is crying (or after coughing) as rales and bronchial breathing may not be audible during light breathing (coughing may be

produced in the young child by slight sudden pressure on the trachea at the suprasternal notch). Respiration often is irregular when the young infant is awake but is regular during sleep. The depth varies greatly. In early life the breath sounds are harsh, loud, and slightly high pitched with expiration prolonged and clearly heard; thus it resembles the bronchovesicular breathing of adults. There is exaggeration of the breath sounds over the bifurcation of the bronchi, immediately to the right and left of the sternum, and posteriorly at the right apex. Vocal resonance is faint but whispered sounds may be more clearly heard and are of some value.

The length, pitch and intensity of both inspiration and expiration should be determined. Rales must be listened for during deep inspiration. Coarse rales often originate in the pharynx or larynx.

No standard can be established for the normal chest in childhood; juvenile characteristics, especially the auscultatory ones, may disappear quite early in some children so that adult findings may be present long before puberty but in most cases there is a gradual transition throughout childhood. Most information is gained from comparing the physical findings on the two sides of the chest, remembering the physiological variations at different ages and in different chest areas.

Common Chest Conditions. These are: atelectasis, acute tracheobronchitis, pneumonia, bronchiectasis, tuberculosis, lipoid pneumonia, foreign body, lung abscess, pleurisy, and empyema.

The Heart. In infancy the heart is large in proportion to the chest; it lies higher and more horizontal in the thorax than in adults. Cardiac dulness therefore may extend as far as 1 to 2 cm. (1 inch) beyond the nipple line on the left. The right border normally cannot be percussed beyond the margin of the sternum In the preschool child the point of maximum impulse usually is in the fourth interspace at about the nipple line; thereafter, it gradually descends to the fifth interspace

Inspection seldom reveals cardiac pulsations in early infancy but later, especially in thin children, they may be quite vigorous. One must look for precordial bulging.

Palpation. Note the point of maximum impulse as well as the distance to the left at which any pulsation can be felt. Thrills should be accurately localized, timed and described.

Percussion. The left cardiac border, after the age of three months, is easily determined by percussion, both above and laterally. Direct percussion is often of value So far as possible careful measurements should be recorded. When the right border can be percussed the heart is enlarged.

Auscultation. The pitch and intensity of the heart sounds must be determined as well as the presence of abnormal sounds and arrhythmias. In childhood the second pulmonic sound (P_2) is normally of greater intensity than the second aortic (A_2). Aortic diastolic murmurs often are best heard in the second and third interspaces to the left of the sternum. Systolic murmurs at the base and over the body of the heart are common and, in [illegible]

tions may occur in children without other evidence of cardiac disease.

HEART MURMURS

Location	*Time*	*Diagnosis*
Apex	Systole	Functional
"	"	Mitral insufficiency
Apex	Diastole	Functional
"	"	Mitral stenosis
Base	Systole	Functional
"	"	Pulmonary stenosis or atresia
"	"	Aortic stenosis
Base	Diastole	Functional (Graham Steell—rare)
"	"	Aortic insufficiency
"	"	Pulmonary insufficiency
Base	Continuous	Patent ductus arteriosus
"	"	Venous hums
Sternum	Systole	Patent interventricular septum
"	"	Tricuspid insufficiency
Sternum	Diastole	Tricuspid stenosis

Common Heart Conditions: (a) *Rheumatic Carditis:* endocarditis, mitral insufficiency, mitral stenosis, aortic insufficiency, aortic stenosis; myocarditis—dilatation, hypertrophy, heart block and pericarditis with or without effusion. (b) *Congenital Heart Disease:* patent interventricular or auricular septum, patent ductus arteriosus, pulmonary stenosis, transposition of great vessels, three-chambered heart, or combination of above. (c) *Post-infectious Myocarditis.* due to diphtheria, scarlet fever, pneumonia, acute nephritis.

The Abdomen. In early infancy the abdomen is slightly rounded and is of about the same circumference as the chest and smaller than the head. The shape soon becomes more rotund as the infant grows. The abdomen should be examined first, while the infant is quiet. Light palpation reveals information as to tenderness and muscle spasm. The *spleen* should be palpated while standing on the right of the patient with the finger tips near the costal margin in the midaxillary line. In the infant the spleen often is lateral and posterior to the position in the adult; in this period a slightly enlarged soft spleen felt just below the costal margin may be normal.

The *liver* size may be determined by placing the left hand under the liver area while palpating the abdomen lightly from the umbilicus to the costal margin with the right hand. Due to the rather marked resistance of the upper right rectus muscle, palpation is best done laterally to this muscle. In infancy, the liver, due to its relatively large size, may normally extend 1 to 2 cm (0.5 to 1 inch) below the costal margin. The upper margin of liver dulness extends to about the fourth rib anteriorly and is determined by percussion.

The *kidneys* can be palpated only when they are abnormally large or the abdominal wall is unusually relaxed. The bladder is not palpable unless it is greatly distended. Deep palpation should be done throughout the abdomen in searching for abnormal masses (e. g., Wilms' tumor, neuroblastoma, congenital polycystic kidney, hydronephrosis, hydro-ureter, congenital megacolon, splenomegaly, hepatomegaly). Percussion is seldom of value except when fluid is suspected. The umbilicus should be examined for evidences of umbilical hernia, and the external inguinal rings palpated in the usual manner. Auscultation over the abdomen is of importance when peritonitis is suspected.

The Genitalia, Male. At birth the foreskin is adherent and daily retraction or circumcision is necessary for proper hygiene. The testicles should be palpated as undescended testicle is not uncommon. One often may be deceived as the cremasteric muscles are quite active and the testicles may be drawn up to the external ring and yet be descended. The size of the testicles should be noted as hypogenitalism is not rare

Common conditions: phimosis, ulcer at urethral meatus, hydrocele, hernia, hypospadias, hypogenitalism

The Genitalia, Female. There usually is a slight mucoid, and occasionally a mucosanguineous discharge from the vagina during the first week of life. Other than slight moisture a discharge after this time is considered abnormal. A mucoid discharge is present at the onset of puberty Vaginal smear at this time begins to show large epithelial cells as compared to the small round cells of the child.

Examination should include separation of the labia and inspection of the urethral and vaginal orifices but not digital examination of the vagina.

Common conditions: labial adhesions, vaginitis, foreign body in vagina, rectovaginal fistula.

The Rectal Examination. This often is neglected in infants though it may reveal important information. In small infants the little finger should be used to prevent tearing at the mucocutaneous junction. Extreme tenderness on pressure and the presence of abnormal masses should be noted. In suspected lesions of the lower bowel proctoscopic examination is valuable. A large female cystoscope may be used for this purpose in infants. Perianal sinus, prolapse, polyps and hemorrhoids are rare.

The Lymphatic System. The lymphatic system of the infant reacts to slight stimuli so that many infants show slight localized or generalized node enlargements without apparent cause. Congenital syphilis is suspected when there is unexplained generalized glandular enlargement before the age of six months. The cervical nodes often are slightly enlarged as a result of respiratory infections

The notch above the inner condyle of the humerus contains the epitrochlear lymph nodes They are best palpated by running the index and second fingers longitudinally along this area. Enlargement during the first six months of life suggests possible congenital syphilis The axillary nodes are palpated by placing the fingers firmly in the axillas and rolling the subcutaneous tissues under the fingers. The inguinal nodes usually can be palpated in later childhood.

The Spine and Extremities. When the child's condition and development permit he should be asked to walk and to run across the room and to flex and extend his spine. Curvature, kyphosis, lordosis, limp or flat feet are thus easily noted.

The extremities must be carefully inspected and examined for abnormalities in form and motor function. Comparative measurements in different areas may yield important information. (See examination of muscular apparatus, Chapter XVII, p. 824)

The infant *hand* is small, and is well padded with fat; the fingers are small and thin With growth, the hand assumes a shape in character with the body build. It must be examined for atrophy, arthritic change, and sweating or excessive dryness of the palms. The nails must be inspected for cyanosis and petechiae, and the finger tips and nails for clubbing The

wrists in infancy are well padded with fat which may be mistaken for epiphyseal enlargement.

The *arms* and *forearms* should be compared as to size, as well as muscular development and coordinated movement. The range of motion of the elbow and shoulder joints should be compared on the two sides.

The *lower extremities* of the infant are short as compared to the body length and are well padded with fat; muscle power is poor. A careful comparison is made of the *feet, arms and thighs. Scars, eruptions and deformities* are to be noted. The patient should be instructed to stand on one and then on the other foot so that the plantar arches may be observed under stress and at rest. The *toes* should be palpated for joint motion or painful enlargement, and the *ankle joint* movements compared as to freedom of motion, pain and enlargement. Edema is first evident in the region below the external malleolus and the forefinger should attempt to pit this area.

The shape of the bones of the *leg* should be noted and the muscles compared for size and symmetry. In infancy the mass of muscle and fat on the outer posterior area of the leg is often mistaken for bowing. Bowing of the tibia (rickets) or saber shin (syphilis) are to be noted. Saber shin consists of spindle-shaped thickening of the middle third of the tibia which also has a roughened edge and slight anterior bowing. Leg ulcers may be found in Negro children due to sickle cell anemia. The musculature of the legs should be compared and the strength tested in various movements. Enlargement of the calves is common in muscular dystrophy and atrophy often follows poliomyelitis.

The knee joints should be examined as to size (enlargements are commonly due to rheumatic fever, tuberculosis or syphilis, trauma, rheumatoid arthritis) and function. The patellas should move freely from side to side and should be smooth in contour.

The *thighs* normally may vary slightly; the shape, condition of the skin, superficial veins, muscles and movements of the hip joints should be observed and compared. The gluteal regions should be compared as to muscular development, scars and eruptions. X-ray examination is indispensable in the diagnosis of bone and joint diseases, and should be routinely employed *in any child with persistent bone pain or who limps.*

Neurological Examination. The neurological examination of the infant or young child is limited by the child's ability to cooperate; the older child can be examined in the same manner as the adult. On examining patients in the early age groups where cooperation is restricted or unobtainable, the importance of observing the infant at play and in motion cannot be stressed too much, since it is often the only way in which abnormal movements can be detected. When the child can walk or run he must be made to do so. Interesting toys should be at hand to stimulate play. Painful or alarming procedures should not precede observation for neurological disorders.

Cranial Nerves. The function of each nerve should be tested as follows:

I. Sense of smell cannot be tested under three years of age. Beyond this age, ask child to identify familiar odors, as peppermint and cloves, with each nostril.

II. Visual acuity may be tested after three years of age, using pictorial charts if the child cannot read letters. The visual fields may be tested in older children by any of the usual methods. Ophthalmoscopic examination is usually disturbing to a child and should be postponed until the end of

III, IV, VI. Eye movements, and nystagmus, if present, can be observed after the age of three months by having the infant gaze at a bright object while the head is suddenly turned. After two years weakness of the extraocular muscles can be detected by having the child, with one eye covered by the examiner's hand, look at some distant object which necessitates paralleling the visual axes. The hand covering the eye is quickly removed and the position of that eye is noted; if it is looking in the same direction as the other eye, it is probable that no imbalance exists. The same maneuver is repeated, covering the other eye. During the first month, and occasionally longer, the ocular movements are normally incoordinate and the child may appear to have an inconstant squint Weakness of the individual extraocular muscles is best elicited while carrying each eye independently through a full range of motion in various angles of gaze.

Reaction of the pupil to light is determined in the infant as in the adult; reaction on accommodation may be tested in the cooperative child after two years of age by converging the gaze on a near object

V. *Motor*· Palpate temporal and masseter muscles while child bites on an object. Look for deviation of the jaw; paralysis of the pterygoid muscles causes deviation toward the affected side.

Sensory: Impossible in infant or young child except for gross pain tests.

Corneal Reflex: Touching cornea (not lashes) with a fine wisp of cotton normally results in prompt blinking

VII. Observe facial musculature on crying and smiling Taste cannot be tested in a young child. Supranuclear lesions of the facial nerve produce no change in the upper facial nerve (forehead) whereas nuclear and infranuclear lesions result in involvement of the upper facial nerve

VIII. *Cochlear Portion* Hearing is difficult to test in the infant; loud noises should startle him. After six months the infant may turn his head in the direction of a loud watch tick. The distance at which a watch may be heard is a rough test of hearing in the older child. In older children the Rinne test may be performed by placing a vibrating tuning fork against the mastoid bone; when no longer heard here (bone conduction) the vibrations should still be audible when the fork is held near the external auditory meatus (air conduction). Bone conduction better than air conduction usually indicates middle ear deafness.

Vestibular Portion The mechanism of equilibrium is complex with the cerebellum, eye muscles, general muscle sense, and vestibular apparatus participating. The function of either labyrinth can be tested separately by caloric stimulation (Figs. 132 and 133). Before this is done it should be ascertained that the ear drums are intact. Irrigation of one ear with cold water normally causes horizontal nystagmus with slow phase toward the same side accompanied by a tendency to fall toward this side and marked vertigo.

Irrigation with warm water produces the opposite effect. Failure to obtain a normal vestibular response indicates a non-functioning vestibular apparatus.

IX, X. The ninth and tenth cranial nerves, being interrelated in function,

gland. The vagus is the motor nerve of the pharynx and larynx and supplies the principal parasympathetic innervation to the thoracic and abdom-

inal viscera. Practically, the neurologic examination of these two nerves is confined to their functions in innervating the pharynx and larynx. On phonation the soft palate should be elevated symmetrically and the uvula should remain in the midline. Local scarring following tonsillectomy may produce pharyngeal asymmetries. A gag reflex is usually elicited by touching the posterior pharyngeal wall on either side with the tongue blade, but this is not always present in normal individuals. If laryngoscopic examination is possible, the vocal cords should approximate the midline. Unilateral lesions usually cause no symptoms, except perhaps slight hoarseness and difficulty in coughing. Bilateral paralysis is always associated with aphonia, marked difficulty in swallowing, regurgitation of fluids through the nose, and loss of the cough reflex.

XI. The spinal accessory nerve is not entirely a cranial nerve, since most of its motor fibers originate in the upper segments of the cervical cord It supplies the sternocleidomastoid muscle which may be seen and felt as the head is turned to the opposite side; if it is paralyzed the head may still be turned by other muscles. The trapezius elevates the shoulder and helps to fix the scapula during abduction of the arm to 90 degrees. Paralysis causes drooping of the shoulder and outward rotation of the scapula. The shoulder can be elevated, however, since the upper third of the trapezius receives supplementary innervation from the third and fourth cervical nerves, whereas the lower two thirds are innervated solely by the spinal accessory.

XII. The hypoglossal is the motor nerve of the tongue The tongue should protrude in the midline and should be freely movable in all directions. With unilateral paralysis the tongue deviates toward the side of the lesion.

Motor System: In the child who cannot cooperate, observation of spontaneous movements at play and in response to tactile stimuli will give satisfactory information about motor function. Any awkwardness, disinclination to use a limb, tremor, or adventitious movements should be noted. Muscle tone is tested by passive movements of the joints. The muscles of the extremities are inspected for size and shape and tested for strength. The infant must be crying and resisting to determine muscle power, but older children can be induced to carry out various movements and assume postures which will indicate the relative strength of muscle groups. These tests must be performed against a moderate resistance exerted by the examiner.

Reflexes: The usual tendon and superficial reflexes (biceps, triceps, patellar, Achilles, abdominal, cremasteric, plantar) are best elicited while the infant is asleep or quiet and before the older child becomes alarmed. [illegible]

[illegible] the time at which the infant can walk without aid. Grasp reflexes in the hands and feet are normally present in young infants.

Sensory Examination: This is impossible until two to four years of age. The response to pin prick, however, will determine the presence of gross pain sensation in the infant.

Coordination: In the infant, coordination can be tested only by observing spontaneous movements of the extremities. Observation of the gait is of value. The usual coordination tests become possible after the third year.

In all testing, experience in evaluating the normal child is necessary. The mother's observations are often a valuable source of information.

Common Conditions of the Nervous System. These are: meningitis (meningococcic, tuberculous, influenzal, streptococcic, pneumococcic, staphylococcic), brain abscess, brain tumor, trauma, poliomyelitis, encephalitis, mental retardation, speech disturbances, idiopathic epilepsy and tetanus.

By Ernst P. Boas

XXIII

THE AGED

Elderly patients constitute an ever increasing portion of the physician's practice, because of the steady aging of the population of the United States. Yet it may well be asked in what manner diagnosis in the aged differs from diagnosis at other ages, and whether the differences are sufficient to justify a special chapter on the problems of diagnosis of persons in the later years of life. When does old age begin? Does geriatrics constitute a legitimate specialty of the practice of medicine? The diseases of the aged are the same as those encountered in the earlier years of life, but the aging person and his reaction to disease differs from the younger person under similar circumstances. Geriatrics, much like psychosomatic medicine, represents a point of view rather than a specialty. It is this point of view, based on knowledge of the aging process and on the physical, emotional and mental reactions of the aging body to disease that comprises geriatrics and that will be set forth in the following pages.

Aging vs. Disease. The chief source of error in the diagnosis of disease in the aged is the assumption by the physician that the complaints and disorders exhibited by the patient are the inevitable and inexorable consequences of aging, and that therefore nothing can be done to relieve them. All too often this conclusion is communicated to the patient, who is told that he might as well accept with resignation the expected disabilities proper to his advancing years. Persons rarely die of old age. Autopsy studies of individuals who have died at advanced ages invariably reveal a disease process responsible for the death Dissolution from mere senility is most exceptional On the other hand, the common stigmata of aging such as loss in weight and in stature, loss of elasticity of the skin and other tissues, loss of elasticity and dilatation of the arteries and veins, thinning and graying of the hair, and presbyopia offer no great hazard to life, and do not cause death. Arteriosclerosis, almost universally accepted as a sign of aging of the arteries, occurs in young persons as well, and is often minimal in the elderly. The first principle of diagnosis in the aged, therefore, is to attempt to distinguish between the manifestations of aging and of disease, and to regard any distinct deviation in structure or function as evidence of ill health, not as a simple manifestation of aging.

Multiple Diseases. It is commonly taught that the most accurate diagnosis is one which embraces all the phenomena of disease in an individual under one cause. This principle is a useful guide in the diagnosis of acute diseases in younger persons, but often leads to error in older patients With the passage of years, breakdown and disease may appear in several organs or organ systems simultaneously or successively. Patients with coronary artery disease often have peptic ulcer as well, and it may be difficult to

determine the nature of their epigastric pain. Symptoms of abdominal distress may be attributed to silent gallstones discovered by roentgenography and a carcinoma of the stomach or bowel may be overlooked. Dyspnea in a patient with hypertension may be due to pulmonary emphysema and not to a failing heart. A rapid pulse in a patient with organic heart disease may be caused by an occult hyperthyroidism and not by a failing myocardium. Thus the physician should not only be prepared to accept multiple causes for his patient's symptoms, he should actually be on the look-out for more than one disease condition in the same patient.

The Need for Exhaustive Diagnosis. Because of the fatalistic attitude that most physicians, as well as patients and their families, hold in regard to the disabilities and diseases of the aged, diagnosis is apt to be slipshod, and detailed studies, such as roentgen studies, are apt to be omitted It is assumed in advance that the outlook is hopeless and that even if a diagnosis were made, therapy would be useless. I have seen persistent vomiting in a woman of 93 attributed to cancer of the stomach, when roentgen study finally revealed a peptic ulcer that yielded to treatment, a grave paranoid psychosis in a woman of 80 regarded as hopeless until electric shock therapy restored her to useful life as matriarch of the family.

Approach to the Patient. Elderly persons are often slow moving and slow thinking; they may be set in their ways and cannot be hurried. Diagnosis in these patients calls for much patience and leisurely methods Their complaints must be listened to at length, and the examination must be painstaking and thorough. An evaluation of their emotional and mental outlook, as well as of their relationships to their families and friends, their activities and their capacity to work should be included The whole examination is aimed, not alone to make an anatomical diagnosis, but to discover abnormalities of bodily function or emotional state that can be corrected or relieved, to enable the aging person to take his place as a useful member of society.

THE AGING PROCESS

Aging is a term that is very loosely employed. Strictly speaking, aging begins at the time of the fertilization of the ovum. It is an error to establish a specific or even an approximate age period at which the body begins to run down. It is true that with the years the body tissues and organs change, imperceptibly at first, but after age 60, perhaps, the summation of these changes brings about a state that we call aging of the body. An estimate of this aging process can be arrived at by physical diagnosis

General Inspection and Review of the Patient. The general appearance and reactions of the patient give valuable clues. It is not alone the color of the hair, and the wrinkling of the skin that reveal the stage of advancement of the aging process. It is rather the impression one gains of the patient as a whole. The *posture,* whether erect or stooped, the elasticity and briskness of gait, the vivacity or deliberateness of movement and of speech, the neatness of the clothes and of bodily hygiene, the degree of attention and interest the patient displays, all reflect in some measure the progress of the aging process

Weight. With age there is usually a progressive decrease in weight which may be physiological, but rapid loss in weight should never be attributed to aging, but should stimulate a painstaking search for possible causes.

Skin. Because of the loss of subcutaneous fat, and the disappearance of the elastic tissue, the skin becomes thin and wrinkled, turgid and non-elastic. When it gets very thin it becomes shiny and smooth. Pallor of the skin is very common, and is often caused by diminished blood supply resulting from disappearance of many cutaneous capillaries. Before assuming the presence of anemia, the physician should estimate the hemoglobin content of the blood. Atrophy of the hair and sweat follicles induces dryness of the skin, which is one of the causes of senile pruritus. Seborrheic keratoses—slightly elevated, greasy flat, yellowish-brown plaques—appear particularly on the trunk and face but have no clinical significance. There is great variability in the time of appearance of baldness and graying of the hair. In women hair may appear on the upper lip and chin.

Teeth. By the time they have reached advanced age, most persons have lost many or all of their teeth. The causes for this do not reside in the aging process alone, for disease plays an important part. Impairment of chewing power plays a significant role in the development of nutritional and digestive disorders, so special attention should be given to a study of the patient's dentures.

Ears. Impairment of hearing, particularly for high tones, begins at age 50 and slowly progresses It is due to simple atrophy of the nerve and the end organ in the cochlea, and is an almost universal accompaniment of aging. The adequacy of hearing should always be checked, for with the use of hearing aids, this deficiency can often be corrected.

Eyes Because of the loss of retro-orbital fat the eyes become sunken, the upper lids often droop from loss of muscle tone. Presbyopia, a constant accompaniment of aging, is due to progressive loss of elasticity of the lens which calls for greater efforts of accommodation on the part of the patient, with eventual inability to focus on nearby objects. It often commences in the fifth decade. There seems to be a correlation between the age of onset of presbyopia and aging, for those who develop presbyopia at early ages die younger on the average than those in whom it develops late. Cataract is common in the elderly but is not due to aging alone. The so-called arcus senilis is seen with increasing frequency in the older age groups, but it too is not a pure senescent process. It is encountered in 15 per cent of persons under age 50. The arcus is a cholesterol deposit in the cornea, and is encountered in young persons who have hypercholesterolemia

Calcification of the *costal cartilages* is usually far advanced after the age of 65. It begins in the second decade of life, and increases steadily with each decade. The bones undergo gradual decalcification and osteoporosis. This is evident in roentgen films which show loss of calcium and changes in the bony architecture. This finding is important for it explains the increased susceptibility of the aged to fractures. Compression fractures of the vertebrae are very common, and fractures of the neck of the femur notorious in their frequency.

The *heart* a[illegible]
physical signs. [illegible]
such as arterios[illegible]
greater frequency in the aged, but this is not due to aging as such, but to the cumulative effect of years of exposure to noxious influences. Abnormal electrocardiograms should always be interpreted as evidence of disease. With simple aging the arteries lose their elasticity and become dilated.

This is especially manifest in the aorta, and dilatation of the aorta in an old person is to be expected. The blood pressure does not rise consistently with advancing years, and many old persons have normal arterial tension. A moderate rise in systolic pressure may result from the dilatation of the inelastic aorta.

Physiological Changes. The most constant bodily changes that come with aging are not manifest by gross organ abnormality, but rather by impairment of function. The normal aging body can function adequately as long as it is not overtaxed. It is the reserve power of the organs, and of the physiological adaptations that are lost. The kidneys have a lessened urea clearance, but can take care of the ordinary demands placed upon them So it is with the heart which adequately meets the tasks set for it by the slowing processes of the aging body—but will not respond to excessive demands. The vital capacity is lowered with advancing years. The sugar tolerance test shows a greater rise in the blood sugar and a delay in its return to normal. The power of homeostasis, of maintaining a constant internal environment of the body under untoward circumstances, is impaired. Thus many of the weaknesses of the aging organism are revealed only when it is put to the test of overloading.

Mental and Emotional State. Many of the mental and emotional changes manifested by elderly patients are due not to the regression of mental faculties with the years, but to the patient's reaction to a life of inactivity, dependency and uselessness forced on him, all too often, by the customs of our society. Thus the physician should inquire carefully into the social and occupational background of the patient, for this may reveal causes of mental and emotional imbalance that can be corrected

DIAGNOSIS OF DISEASE IN THE AGED

A knowledge of the frequency of disease is a distinct aid in diagnosis. Mortality tables alone do not reflect an accurate picture of the incidence of disease, for many disorders are incapacitating without causing death. The most common causes of death after age 60, in the order of their frequency are:

Cardiovascular renal diseases
Cancer
Accidents
Influenza and pneumonia
Diabetes
Tuberculosis

The national health survey carried out by the United States Public Health Service in 1935 revealed the following prevalence of chronic diseases in the order of their frequency.

Rheumatism
Heart diseases
Arteriosclerosis and high blood pressure
Hay fever and asthma
Hernia
Hemorrhoids
Varicose veins
Chronic bronchitis

Nephritis and other kidney disease
Nervous and mental diseases
Goiters
Cancer and other tumors
Diseases of female organs
Tuberculosis—all forms
Diabetes mellitus
Diseases of the gallbladder and liver
Ulcer of stomach and duodenum
Diseases of bladder and urethra

A study of hospital discharges in New York City in 1933 disclosed the following chief conditions responsible for hospitalization:

Heart diseases
Vascular diseases
Malignant neoplasms
Cerebral arteriosclerosis, hemorrhage
Fractures
Cataract
Diabetes
Bronchopneumonia
Non-malignant neoplasms
Arthritis
Tuberculosis
Lobar pneumonia
Appendicitis

In the later years of life the acute infectious diseases, with the exception of the pneumonias, are of less importance as causes of illness. It is the chronic so-called degenerative diseases that are the chief causes of disability and death Even tuberculosis and syphilis, when they appear or persist in an aged person, are chronic and indolent in their course.

In the following pages we shall consider the diagnosis of disease in the aged, not the aging process as such. The methods of diagnosis do not differ from those employed for patients of other age periods, so no attempt will be made to present an exhaustive inventory of diagnostic methods. We shall try rather to emphasize the important conditions encountered in the elderly and the errors that may arise from overlooking their manifestations

General Appearance of the Patient. One should note the nutrition and weight of the patient Loss in weight may be the first manifest sign of hidden disease, most often neoplasm or hyperthyroidism. The nutritional state may reflect disorders of the gastro-intestinal tract or of the teeth, or may indicate a vitamin deficiency Special attention should be paid to the appearance of the tongue which so quickly reflects an inadequate intake of elements of the B complex Cheilosis, the macerated lesion at the angles of the mouth, may testify to a deficiency in riboflavin, but more often is caused by drooling at the corners of the mouth resulting from poorly fitting artificial dentures that allow the upper lip to overhang the lower Obesity is not so common in the aged, but if present calls for correction. The hemoglobin should always be checked, because the color of the skin is a very deceptive guide to the presence or absence of anemia. Attention should be paid to the gait of the patient and to the presence or absence of tremors—early indicators of Parkinson's disease or of involvement of the extrapyramidal tracts. The mental capacity, and emotional reactions of the patient should be estimated. The general survey of the patient should always include

palpation of the lymph nodes. Regional enlargement may give the first evidence of a malignant neoplasm. Generalized enlargement is an indication for a complete blood count, for chronic lymphatic leukemia is not uncommon in the aged. In measuring the temperature, the thermometer reading should always be made by rectum. Small rises in temperature in the aged are often significant.

Eyes. Blepharitis and conjunctivitis are common The pupils of the aged are often myotic and react feebly to light. Such a reaction should not heedlessly be attributed to cerebrospinal syphilis. Cataract should always be sought for. Most often overlooked is glaucoma The tension of the eye balls should always be tested by palpation, and if any symptoms such as blurring of vision or pain in the eyes are present, careful tonometric measurements are indicated.

Lungs. The thoracic cage of the aged person is rigid, the costal cartilages, as revealed by roentgen ray, calcified, and the chest moves up and down as one unit. Pulmonary emphysema is very common. It is characterized by prolonged, low pitched expiration, and on fluoroscopy and x-ray by increased aeration of the lung fields Air cysts of the lung, which are nothing but huge emphysematous blebs, can be recognized only by roentgen ray examination, and are easily confused with pneumothorax. Chronic recurring bronchitis occurs as a rule in emphysematous lungs. Many such patients have persistent coarse moist rales at the bases The presence of pulmonary emphysema often masks the physical signs ordinarily associated with other pulmonary disorders such as tuberculosis or neoplasm or even a pleural effusion. That is why x-ray studies are indispensable as a supplement to physical examination.

Chronic fibroid tuberculosis is frequent in old persons whose persistent cough is attributed to chronic bronchitis Such cases account for much familial infection, particularly of children In the absence of major scarring and cavitation, the physical signs may be just those of emphysema with some pulmonary fibrosis and rales diffusely scattered throughout the lungs. Roentgen examination is needed to reveal the true state of affairs. In all cases of chronic cough repeated sputum examinations for the tubercle bacillus should be done

Neoplasms of Lung. Any unilateral pulmonary lesion in an older person should suggest the possibility of neoplasm The early symptoms are not characteristic—cough and pain in the chest, more rarely hemoptysis. These tumors are usually endobronchial and therefore cause atelectasis of the portion of lung peripheral to the tumor The first physical signs consequently are dulness and diminished breath sounds. Early bronchial stenosis may be suggested by wheezing rales that persist in a specific area of the chest. Careful palpation of the lymph nodes above the clavicle, particularly those behind the origin of the sternomastoid muscle, may reveal metastatic deposits which by biopsy may lead to the correct diagnosis. In all cases careful roentgen study and bronchoscopy are indicated. Metastatic tumors of the lung often exhibit no physical signs and are discoverable only by roentgen examination.

True bronchial asthma of the allergic type is not common in the aged. Chronic bronchitis with infectious asthma is very frequent. In acute attacks, usually brought on by pulmonary infection, wheezes as well as moist rales are heard throughout both lungs. With recovery the wheezes become min-

imal, but the coarse moist rales often persist in the lower lobes, and these lung fields may also exhibit dulness. Dyspnea and cyanosis are common features of this disorder, and the problem often arises to what extent they are conditioned by the heart and to what degree by the pulmonary lesion. The size of the heart is a valuable guide in reaching a conclusion. In the absence of cardiac enlargement, particularly of enlargement of the left auricle, heart failure is unusual. The size of the heart should always be determined by fluoroscopy, for the emphysematous lung makes it impossible to delineate the cardiac borders by percussion. Similarly it may be difficult to distinguish between an asthmatic seizure and acute left ventricular failure with paroxysmal dyspnea. Further confirmation may be found by measuring the circulation rate by means of decholin or calcium gluconate A normal circulation time indicates that the dyspnea is pulmonary in origin.

Lipoid pneumonia, caused by inhalation of unassimilable oils, usually mineral oil, may lead to errors in diagnosis. This condition gives rise to few symptoms and the physical signs are not characteristic. The roentgen film may show linear or nodular infiltrations that may coalesce to form larger areas of consolidation in the lower lobes. The roentgen picture may simulate bronchiectasis, basal tuberculosis, or pulmonary neoplasm. At times diagnosis can be made by discovering oil droplets in the sputum.

Elderly, bed-ridden patients commonly develop pulmonary inflammation and fever. The differential diagnosis between bronchopneumonia and pulmonary embolism should invariably arise in the mind of the physician. The physical signs are of little help in differentiation, for hemoptysis and pleural friction rub do not commonly accompany pulmonary infarction Based on the knowledge that phlebothrombosis of the legs and pulmonary embolism are almost universal in old persons who have been confined to bed, the presumptive diagnosis should be pulmonary embolism. Careful inspection of the leg veins may reveal local thrombosis as the source of embolism.

Heart. For the diagnosis of cardiac conditions, and in particular for an estimation of the functional capacity of the heart, symptoms are as important, if not more so, than physical signs. It is a truism that a person can have advanced coronary artery sclerosis with a heart of normal size, good heart sounds, no murmurs and a normal electrocardiogram. In all cases the symptoms should be correlated with the objective findings. It has been pointed out in previous paragraphs that advanced pulmonary disease may simulate cardiac dyspnea and cyanosis. Similarly edema of the legs may be due to extracardiac causes, and this occurs with particular frequency in the aged. Varicose veins of the leg, malnutrition with lowering of the blood proteins, and severe anemia are common causes of swelling of the legs. Abdominal tumors blocking the venous and lymphatic return from the legs are another cause.

The quality of the heart sounds is often of diagnostic significance. In the absence of obesity or advanced pulmonary emphysema feeble heart sounds suggest myocardial disease. Of particular importance is correlation of the size of the heart with the loudness of the first heart sound. If the heart is large and the first sound faint or dull, myocardial disease can be diagnosed with assurance. The heart rate in elderly persons tends to be slower than in younger individuals so that tachycardia becomes of greater significance.

The carotid sinus reflex is more active in older persons particularly in the presence of coronary arteriosclerosis. Such hyperactivity may account for fainting spells.

Murmurs of the so-called functional variety are unusual in older patients. Systolic murmurs are, as a rule, of little clinical significance in spite of the fact that they are caused by cardiac abnormalities. Systolic murmurs at the aortic area are usually due to simple dilatation of the aorta accompanying arteriosclerosis or hypertension. Systolic murmurs at the apex are caused by atherosclerosis of the mitral valve or ring, or by a relative mitral insufficiency. *If the patient is febrile, any murmur should arouse the* suspicion of subacute bacterial endocarditis which may occur in the aged.

A harsh loud systolic murmur at the aortic area usually is a sign of calcareous aortic stenosis. In advanced cases a systolic thrill is palpable *The mitral diastolic murmur of mitral stenosis may indicate a very old* indolent rheumatic valvular lesion or else calcification of the mitral ring with resultant narrowing.

Aortic insufficiency most often is due to an atherosclerotic valvular lesion or to a relative insufficiency resulting from extreme hypertension. At this age syphilitic and rheumatic aortic lesions are not very common.

Cardiac Irregularities Extrasystoles are very common and have little clinical significance except when they are associated with certain other conditions. In the presence of an acute infection, or when associated with frequent anginal seizures or myocardial infarction they suggest injury to the myocardium. Multifocal extrasystoles, that is extrasystoles arising in different regions of the myocardium and characterized by differing electrocardiographic configurations, suggest myocardial disease Auricular fibrillation, when occurring in a patient with a large heart has the same significance as in younger persons When the cause of auricular fibrillation is not apparent, and particularly when the ventricular rate is rapid, hyperthyroidism should always be suspected Auricular fibrillation may occur in old persons without valvular disease, hypertension, cardiac enlargement or hyperthyroidism. Its cause is not definitely known, and should not lightly be assigned to arteriosclerotic heart disease. Auricular flutter and paroxysmal tachycardia are not very common in the aged. Paroxysmal ventricular tachycardia may follow myocardial infarction. It is a very grave complication which can be recognized with certainty only by the electrocardiogram. Partial or complete heart block as well as intraventricular block and bundle branch block give evidence of myocardial damage almost invariably due to coronary artery sclerosis. These disturbances of conduction, for the most part, can be diagnosed only by means of an electrocardiographic tracing. They may occur in the absence of manifest symptoms of cardiac disturbance. An electrocardiogram should constitute a routine part of the complete examination of an elderly patient.

Hypertension in the aged is usually benign and well tolerated, even when it is maintained at rather high levels Knowledge of both systolic and diastolic pressures is needed to evaluate its significance. Systolic hypertension, in which the diastolic pressure remains unaltered, and the systolic pressure measures from 150 to 170 mm Hg. should be sharply differentiated from diastolic hypertension. Systolic hypertension results not from increased peripheral resistance due to narrowing of the arterioles, but from dilatation and loss in elasticity of the aorta. It does not place an added burden on

the heart and is of no clinical significance. In diastolic hypertension both systolic and diastolic pressures are elevated proportionately. The increased pressure places a load on the heart which hypertrophies, and also accelerates the development of arteriosclerosis.

Elderly patients with hypertension eventually succumb to heart failure, myocardial infarction, cerebrovascular insults or renal insufficiency. The presence of the anginal syndrome, evidences of heart failure, or great cardiac enlargement point to illness and death from cardiac causes. A very high diastolic blood pressure, severe headaches, transient aphasia or palsies portend a cerebrovascular accident. Renal insufficiency is the least common sequel. The sufficiency of the kidneys can best be checked by determining their ability to concentrate the urine. If the specific gravity of the urine is fixed at a low level, determination of the blood urea nitrogen will reveal the degree of renal impairment.

Thickening and arteriosclerosis of the radial and temporal arteries is of little clinical significance, and does not permit the conclusion that the visceral arteries are similarly involved. Beaded calcified radial arteries, and other calcified arteries of the extremities that may be discovered by roentgenograms represent the Monckeberg type of medial calcification which does not lead to arterial obliteration or disease. Careful palpation of the femoral, popliteal, posterior tibial, and dorsalis pedis arteries should always be carried out. Absence of pulsation is encountered particularly in the posterior tibial and dorsalis pedis arteries It indicates obliterative vascular disease and is often associated with symptoms of intermittent claudication or trophic disturbances of the extremities. The discovery of absent or feeble pulsation in these vessels should lead to oscillometric studies of the arteries of the lower extremities to determine the extent of the vascular occlusion.

Etiologic Considerations. Arteriosclerosis of the coronary arteries is responsible for the great majority of heart conditions in older persons. Early diagnosis depends more on the symptomatology than on objective findings. It cannot be emphasized too often that serious coronary disease may exist without any physical or electrocardiographic signs of cardiac involvement. In the presence of diabetes mellitus suggestive symptoms should be accorded greater significance, because of the great frequency of arteriosclerosis in diabetics of long standing. Physical examination and electrocardiography will not reveal the functional adequacy of the coronary circulation; this can be estimated only from the symptomatology. The exercise test, in which an electrocardiogram is taken at rest and again after physical exertion that falls just short of giving rise to anginal symptoms, may disclose a latent inadequacy of the coronary circulation. When such exercise is followed by significant depression of the RST segments in several leads coronary insufficiency is made apparent.

Myocardial infarction is often overlooked or mistakenly diagnosed as a simple attack of angina pectoris Whenever a patient with coronary disease experiences an abrupt change in the pattern of his anginal pain, or when a patient, previously in good health, suddenly develops the anginal syndrome, the physician should assume that there has been a myocardial infarction until he has ruled it out with all available diagnostic tests. Repeated electrocardiograms should be taken and multiple chest leads should be employed. For ordinary clinical use the routine use of chest leads V_2, V_4, and V_5 is sufficient. Within twenty-four hours of a myocardial infarction

constitutional symptoms resulting from necrosis of the heart muscle ensue, and should always be sought for. They are fever, leukocytosis, and an increase in the sedimentation rate of the red blood cells.

Fortunately the term "chronic myocarditis" which used to be applied indiscriminately to hearts of older patients has been discarded. But in its place has crept the term "arteriosclerotic heart disease." Arteriosclerotic heart disease should be diagnosed only when there is definite evidence of arteriosclerosis of the coronary arteries or of the valves. The diagnosis of coronary artery sclerosis rests on the presence of the anginal syndrome or electrocardiographic evidence of myocardial damage not caused by any other lesion. Cardiac enlargement in old persons, in the absence of hypertension or of valvular disease, is usually due to repeated myocardial infarcts. The heart sounds are faint in comparison to the size of the heart, the pulsations of the left border of the heart may be very small, and at times there is paradoxical pulsation—a part of the left border bulges during systole. This phenomenon is caused by thinning of the heart muscle in the region of a healed infarct, and, if well marked, may denote an aneurysm of the heart Electrocardiograms of such large hearts usually give evidence of extensive myocardial damage.

Heart failure in old persons with hypertension or coronary artery disease is usually left ventricular failure Because pulmonary and hepatic engorgement and edema of the legs may be lacking the failure is often overlooked. Dyspnea is the first evidence of left heart failure. Confirmation can be found in fluoroscopy which will demonstrate engorgement of the pulmonary arteries, and usually dilatation of the left auricle. In doubtful cases determination of the circulation time will give the desired information.

The most characteristic valvular lesion in old persons is calcareous aortic stenosis This is usually a solitary valve lesion which may be associated with aortic insufficiency. It is marked by a rough systolic murmur at the aortic area often, but not always, accompanied by a systolic thrill In advanced cases the pulse is small and slow The association of the anginal syndrome or partial or complete auriculo-ventricular block with such findings confirms the diagnosis. The heart is enlarged and there are electrocardiographic evidences of left ventricular strain or of myocardial damage It is believed today that calcareous aortic stenosis develops on an old rheumatic valvular lesion. Any other rheumatic valvular lesion may be encountered in old people

When a prolonged febrile condition occurs in an old patient with a valvular lesion, or with an unexplained systolic murmur, subacute bacterial endocarditis should always be ruled out by means of a blood culture Both subacute bacterial endocarditis and rheumatic carditis are not very infrequent among elderly persons

Syphilitic Lesions of the Aorta. Aortic insufficiency, aneurysm, and stenosis of the orifices of the coronary arteries with the anginal syndrome are uncommon in persons of advanced ages, but the possibility of their occurrence should always be entertained. The Wassermann or Kahn test [illegible] ospinal

[illegible] atten-
tion should be directed to his general nutrition and to the presence or absence of anemia. It is well to check the blood proteins. Malnutrition, hy-

poproteinemia and anemia often result from the prolonged invalidism of heart failure and contribute to myocardial weakness and edema formation

GASTRO-INTESTINAL TRACT

Routine physical examination and palpation of the abdomen are of little aid in the early diagnosis of gastro-intestinal disorders. A rectal examination should never be omitted. It may disclose a neoplasm of the rectum or of the prostate. Since carcinoma is such a common occurrence in all parts of the gastro-intestinal tract of older persons, and since its early diagnosis is so important, and at the same time so difficult, it should be searched for painstakingly in every case in which there is the slightest question as to the nature of the disorder. Most errors in diagnosis are errors of omission. Difficulty in swallowing, indigestion, heart burn, a change in the bowel habits may be due to benign causes, but this may never be assumed until an exhaustive search has ruled out the presence of a neoplasm. This means that every such case should be subjected to careful roentgen study of the gastro-intestinal tract by an expert in the field. This should include a study of the esophagus, the stomach and intestines, with particular attention to the cardiac region of the stomach, the small and large intestines. Careful record should be kept of the patient's weight. Loss in weight is always significant. The gastric contents and the stool should be examined for fresh and occult blood. A complete blood count may reveal anemia, or leukocytosis, and the sedimentation rate may disclose a hidden disorder.

A gastric ulcer discovered by roentgen examination should be assumed to be cancerous until proven otherwise. In most cases gastroscopy is indicated. The roentgen examination should be repeated after a few weeks of intensive treatment to discover whether or not the ulcer has healed. Lack of healing should arouse suspicion of cancer. The presence of blood in the stool or of symptoms referable to the lower bowel is an indication for immediate sigmoidoscopy. Every patient with hemorrhoids should be subjected to sigmoidoscopy for the hemorrhoids often mask a neoplasm higher up.

Peptic ulcer both of the stomach and of the duodenum does occur in older persons Diverticulitis may simulate carcinoma of the sigmoid.

Inguinal and femoral *hernia* occur with increasing frequency in the older age groups. Search for hernias should be part of every physical examination. Incarceration or strangulation of a hernia are common causes of intestinal obstruction and death.

Hepatitis is uncommon in older persons. Jaundice may be due to common duct stone, or to carcinoma of the pancreas, liver, or gallbladder or bile ducts. In the presence of complete biliary obstruction, evidenced by acholic stools and absence of urobilin in the urine, an accurate differential diagnosis is usually impossible, and surgical exploration is indicated. Apparently hopeless cases have been cured by removing stones from the common bile duct

GENITO-URINARY TRACT

The most common disorder of the urinary tract in older men is benign enlargement of the prostate gland. Rectal examination reveals the size of the gland and its consistency, but gives no information as to how much it obstructs the outlet of the bladder. Whenever there is difficulty in urination, the patient should empty his bladder as completely as possible, and

then a catheter should be inserted to measure the residual urine. If the residual urine exceeds 50 cc, a cystoscopy should be done to discover the site and nature of the obstruction, and to determine what operative procedure is best adapted to the case. The kidney function should always be determined. Carcinoma of the prostate may be diagnosed when the prostate gland as felt by rectum is large, hard, and infiltrates surrounding tissues. It should be suspected when very hard nodules can be felt within the gland. If such a hard nodule is discovered, the gland should be exposed by *perineal incision and a portion of the nodule subjected to study by frozen* section. The presence or absence of metastases should be established by determination of the acid phosphatase of the blood Elevation of the acid phosphatase is a certain indicator of metastasis from carcinoma of the prostate.

In women, a routine examination should include careful study of the uterus, ovaries and breasts for cancer. This includes a manual pelvic examination, visual inspection with a speculum and a cytological study of the vaginal smear for tumor cells. Vaginal bleeding calls for curettage and microscopic study of the scrapings if no other patent lesion is found.

BONES AND JOINTS

Osteo-arthritis is the common disorder of the bones and joints in older persons. It is found chiefly in the joints that bear the greatest continuous stresses, namely the knees, the spine, the sacro-iliac joints and the hips. Osteo-arthritis is not caused by infection and should be differentiated from rheumatoid arthritis. Osteo-arthritis is not associated with fever, anemia or an acceleration of the sedimentation rate of the red blood cells. The affected joints show little soft tissue swelling, although they may be enlarged there is no redness Creaking and crepitus of the joints are the rule Roentgen examination reveals narrowing of the joint space, and irregular spur and lip formation around the joint margins The extent of the deformities revealed by roentgen ray do not parallel the symptomatology Many old persons exhibit far advanced osteo-arthritis of the spine, yet have no symptoms, others have disabling symptoms with minimal objective lesions. In all cases of osteo-arthritis special attention should be paid to the weight and posture of the patient, for these mechanically affect the joint lesions. Heberden's nodes are bony exostoses that appear on the proximal ends of the terminal phalanges of the fingers and are often associated with manifestations of osteo-arthritis in other joints.

A solitary arthritis, or gross multiple joint deformities should always arouse the suspicion of gout. Diagnosis is confirmed by the discovery of urate tophi in the ears, bursae (such as the olecranon bursa) and subcutaneous tissues and tendons. Serum uric acid levels of from 6 to 14 mg. per 100 cc. confirm the diagnosis The history of the development of the arthritis is an important diagnostic aid.

Osteoporosis, which can be diagnosed only by the roentgen ray, is important because it is very common, and because it often leads to fractures, particularly to compression fractures of the spine. Pain in the spine always calls for roentgen study.

Paget's disease in its advanced form with deformities of the skull and extremities is recognizable at a glance Weakness and pains in the bones, or at times spontaneous fractures constitute the early symptomatology. The

roentgen study, which should always include the skull and the pelvis as well as the long bones, is diagnostic. In addition the alkaline phosphatase of the serum should be estimated. It is greatly elevated in Paget's disease.

Bone pains should always arouse suspicion of metastatic neoplasms. In the early stages roentgen studies may not reveal any lesions. A rapid sedimentation rate, and an increase in the alkaline phosphatase may be the only signs suggesting neoplasm.

THYROID

Hyperthyroidism is not uncommon in older persons, but it is often overlooked because these patients do not present the classic signs of exophthalmic goiter. There may be no thyroid enlargement, no abnormal eye signs, and even the heart rate may not be unduly rapid. Unexplained loss in weight, diarrhea, or auricular fibrillation should always arouse suspicion of hyperthyroidism. The basal metabolic rate should be determined whenever there is the slightest doubt.

Summary. Basic to medical diagnosis in the aged is a knowledge and recognition of the aging process. The next step is to distinguish between senescence and disease, and to regard gross abnormalities in structure and function of the body as evidence of disease, not of aging. Diagnosis is aided by an awareness of the important diseases that occur in elderly persons, as well as of the fact that commonly more than one disease condition is present in the same patient. Every patient is entitled to an exhaustive examination, for only such an approach makes possible a hopeful and constructive course of treatment.

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By Melvin W. Thorner

XXIV

THE PSYCHIATRIC PATIENT

The suspicion seems to have grown in medicine recently that psychiatric symptoms occur in disembodied people and are only casually related to real people who have hearts, lungs, sunburn, and "athlete's foot." The tradition has been fostered insidiously by those reports of psychiatric patients in the literature of psychiatry where it is often casually stated in case reports that "the physical examination was negative " Such a statement is semantically ambiguous and could mean either that an examination of some sort yielded no helpful information or that no physical examination was done! At most it can mean that the letter of the rule (that all patients must be examined physically) was followed, but with no great enthusiasm for the spirit of inquiry. If the tradition that psychiatry as one branch of medicine which considers a patient from all angles is to be upheld, the physical examination of the psychiatric patient demands more than lip service.

THE PSYCHIATRIC HISTORY

The Chief Complaint

This is a most important point in the psychiatric history It should be noted as nearly in the patient's own words as possible even though the patient may often interpose difficulties. Is should be obtained from the patient whenever possible in some noncommittal way. "What can I do for you?" may be answered with "Nothing, I guess Nobody can do anything for me," by the depressed patient "What is your problem?" may be answered by "Problem? Problem? I don't have any problem that I know of," by the querulous, paranoid patient whose own difficulties are blamed on others. "*What is your chief complaint?*" "*I am not a complaining person,* Doctor I can be practically dead and I won't complain " "What is wrong with you," may meet the classical triumphant retort of patients, "That's for you to find out, Doctor." There is no opening conversational gambit which can serve to avoid such answers in all cases, but though the words of the patient's response are not informative, their manner and character may be. Frequently psychiatric patients have no complaints, and give the doctor to understand that they have come just to satisfy their families. In military or industrial practice, the patient may have unwillingly submitted to an order to appear for a "sanity test " Often the real reason for coming to the doctor is kept under cover, and some substitute is put forth, until such time as the patient feels that the doctor is a person in whom it is safe to confide. In such cases, it is of no use to belabor the point early in the examination,

for the real reason for seeking medical aid will usually appear sometime later. It is unwise to press any point upon a reluctant patient in the early phase of his contact with the doctor, as the antagonisms which may arise from the tussle can be very difficult to overcome subsequently. Sooner or later the doctor should decide just what definite situation it is that culminated in the visit to his office. In dealings with many psychiatric patients, this point is usually known later rather than earlier.

Development

The more formal parts of the history are best looked into first, since once having gone from the formal to the intimate, a return to the formal will prove awkward. The developmental history of the patient as it concerns age at sitting, teething, standing, walking, and talking is usually of interest only in the mentally deficient, but even there it is apt to be misleading if too literal an interpretation is placed on it. Many mentally deficient children have normal physical developmental histories, while a history of retarded early physical development has occurred in many a superior person.

The school history can also be dealt with at this time. Schools vary greatly in their methods and standards, and the passing of a school grade at the normal age is no criterion of average intellectual development. Some schools do not believe in having a child repeat a grade and will advance him no matter what the character of his work. Some superior children become so bored with a type of work that does not constitute a challenge to their abilities that they miss it altogether and fail of promotion. However, a boy who has tried unsuccessfully to pass the first grade of schooling and has retired from the field at the age of sixteen, is almost certainly intellectually inferior. On the other hand, a doctor of philosophy in mathematics of one of the best universities is not likely to be short of adequate intellectual capacity.

The *character of the life* the patient has lived, and his likes and dislikes in the past, are among the high priority diagnostic materials that may come into the doctor's possession. Each person has a different pace at which he lives his life. Some maintain this constant pace of living all their lives, others fluctuate either mildly or wildly. The hobbies of patients are often interesting clues to their likes and aims. The lack of hobbies seen so often in psychiatric patients is likewise important, and such a lack is often an ill omen in that it signifies reduced interest in the outside world. The physical activities of the patient aside from his work are important indications of the ability of the patient to fit in with the social order, as most sports are competitive.* The number and type of social organizations to which a patient belongs may reveal things about him that are unconscious expressions of inner drives. A member of a racial hatred organization will not ordinarily be found to overflow with the milk of human kindness. Interest in people, either of the same or opposite sex, is a potent force in directing an individual's life, and much of subsequent therapy will depend for direction upon this information. The doctor should strive to visualize, in a general sort of way, what manner of person he has for a patient. The picture he forms should be adequate enough so that he can predict (to himself and in

* Baseball is a peculiar exception. Often a lonely, schizoid person has played baseball frequently.

silence) how his patient may react to the simple situations he may encounter in everyday life.

The *family* of which a patient is a part has doubly important meaning in psychiatry. It bears directly on the hereditary constitution of the patient. It also tells what sort of people have influenced the patient in his formative years. The question of the significance of heredity in the psychiatric disorders have never been answered to anyone's satisfaction. There do appear to be a few families in which the majority of the members of all generations have been sick or hopeless from the psychiatric standpoint, but psychiatric patients most often come from families the constitution of which does not suggest any unusual predisposition to mental disorder. Any generation of a family that is sufficiently large is apt to have some very bright members while one or more may be mentally deficient. The schizoid psychoses may spring up anywhere, as may the epileptiform disorders. Some few diseases such as Huntington's chorea, amaurotic family idiocy, Mongolian idiocy, and some of the degenerative diseases show direct inheritance or familial tendencies very markedly.

The *home environment* of a child can exert a great influence in determining what his personality characteristics will be. Most children are brought up in the home of their parents, but many must go elsewhere during their early years. As children develop largely by imitation, they ape the mannerisms, viewpoints, and social theories of the adults and other children about them. This imitation is not unthinking or uncritical, for a child's resentment may lead him to become negativistic and do things by opposites. A very active, overprotective mother is apt to rear a child whose major purpose in life is either revolt or retirement, while a quiet, self-contained mother is likely to bring up children as content and spontaneous as herself Even in an adult the personality characteristics may be largely a response to his family (or family substitute) and their way of living. The effects of this influence of the family interpersonal relationships are inextricably linked with pure heredity in the case of the patient living in the bosom of his family, and it is usually impossible practicably to separate the respective factors for mature consideration

The *occupational history* is important because it often furnishes an indication of the aims of an individual. In the ambitious neurotic the occupational goals may be impossibly high. In the schizoid person a lack of adaptability may manifest itself in an indifferent work history punctuated by many changes of job and locale The mentally deficient are not usually troubled by overweening desires and they select and hold jobs in which routine and repetition are outstanding A work history may be dictated by expediency, however, and unwarranted conclusions might then easily be made. Sometimes poor work histories suddenly turn about and become brilliant. Sometimes the aims of people shift, and sober, hard-working men, like H. G. Wells' Mr. Polly, decide in a moment that the game is not worth the candle, and seek easier pathways than those of unremitting toil. The occupational history may also suggest the possibility of disease of occupational origin The exogenous toxins of lead, manganese, carbon monoxide, and mercury may be encountered in some trades Sometimes the demonstration of such a causative agent as an occupational hazard can entail a very pretty exhibition of medical acuity.

The record of the *diseases* from which the patient has suffered is a part of the history which rounds out the story. Has the patient been ill frequently? Has he ever been entirely free of symptoms? What is his own reaction to the presence of disease? Does he use disease to help him to his own ends? These are some of the general questions which arise concerning the history of illness in a psychiatric patient. A history of specific infectious diseases can be very helpful with some psychiatric patients. It is wise to inquire carefully into food habits and digestive symptoms since psychiatric patients, for reasons connected with their mental difficulties, are often prone to various types of self-imposed dieting which have no medical indication. This is frequently seen in the cultists and fadists among paranoid patients and among some neurotic individuals. The woman who overdiets in a neurotic attempt to attain bewitching and irresistible slenderness is a good example of this. One of the specific end-results of such faulty food habits is the possibility of clinical or subclinical avitaminosis. In the aged, in the dementias, among schizoid patients, and in the toxemias there is often a dangerous neglect of a well balanced diet. Sleep habits, bowel habits, and menstrual irregularities are worth inquiring about for these functions are often menaced by emotional unrest.

The *menstrual history* of women and a *record* of *pregnancies* may be important Menstrual changes are frequently the result of psychiatric disturbances. Some psychiatric difficulties are apt to become more obvious in and around the menstrual periods, and any such cyclic disturbance should be investigated further from the endocrine standpoint. Any of the psychiatric disorders may appear during pregnancy or following labor, but their character is not specific and they may be neurotic upheavals or psychoses which appear to be precipitated by childbearing, or may be merely coincidental with that event The incidence of abortions induced for social and economic reasons in the United States is very large, and it is doubtful that any woman who has an induced abortion for reasons of convenience does so with no enduring mental qualms. Sometimes strong feelings of guilt may be attached to these incidents and almost always there is some regret experienced.

The period of life during which menstrual activities cease is likewise a period in which a changing outlook makes many mental readjustments necessary. The laity and many of the medical profession have been rather too avid in seizing upon the physical evidences of involuting endocrine activity as being directly responsible for a host of mental difficulties. Similar difficulties appear in men of the same age period, and the suspicions

[illegible]

parallel.

Caution should be exercised in questioning patients too closely about any aspect of their sexual life, and one should avoid overemphasis upon its importance by dwelling on it at great length too early during contact with the patient.

No survey of past medical conditions is complete without obtaining a record of definite illnesses of any type, operative procedures, or any accidents, especially when these have involved cranial injury.

OUTWARD ASPECT OF THE PATIENT

The Patient's Clothes

The general appearance of the patient as he steps over the threshold of the doctor's consulting room gives more information than many more time-consuming procedures. His clothes and their state of repair offer some indication of how interested he may be in the world about him. A person whose difficulties weigh so heavily upon him that he can think of little else is not apt to have a spruce, well-groomed appearance. The dress of older people is always interesting in that so many portray an earnest desire for a return to the past by over-youthful types of dress. Many older women symbolize their unwillingness to accept their aging by wearing clothes more appropriate to a girl in college or high school. A young and pretty girl who is not well groomed is obviously not thinking along the romantic grooves sanctified by the travel of hundreds of generations of young and pretty girls, while for a schoolboy a studied carelessness of attire may be merely the current mode. Often people reveal their aspirations in the type of dress they select. For while one cannot easily change his body build or facial appearance, the character and state of the clothes selected are modified only by a patient's inclinations and his pocketbook.

Body Attitude

The general carriage, too, is a feature of the patient susceptible of a wide latitude of individual variation. The stooped shoulders of a patient who is hopelessly immersed in a psychotic depression, or the jaunty stance of the manic patient, may contrast violently with each other, especially when one attitude succeeds the other in the same patient at different phases of his manic-depressive disease. The agitated hand wringing of a patient suffering from a depression of the involutional period is a very eloquent symbol of the furor of self blame which prompts it. The attitude of tense expectancy seen in so many anxiety states is a valuable signpost of the mental disturbance within. Throughout our lives each of us has either consciously or unconsciously observed the association of general body attitudes with the emotional states promoting them. It is not well to look upon evidence of this sort as completely diagnostic in itself, but it helps later on if these impressions are remembered when all the available evidence is gathered together. Less familiar to the experience of those who have had little to do with patients suffering from mental disease are the bizarre attitudes seen in many psychotic patients of the schizophrenic group The significance of such a bizarre attitude may be lost in a labyrinth of transformation and symbols, but its presence may help to establish the diagnosis and nature of a schizoid psychosis.

Gait

The gait and its characteristic changes are often clues to severe disturbances resulting from altered function of the nervous system. This alteration sometimes rests on the basis of a demonstrable pathologic lesion, although in many cases none may be present. Often the measured and peculiarly stiff-legged and shuffling gait of paralysis agitans may be a sign of an encephalitis or its sequels This same encephalitis at higher cortical levels may produce mental symptoms which accompany the gait disturbance. The postural spasticity of the gait of patients with pyramidal

tract lesions may give an important lead to the diagnosis of vascular, degenerative, or encephalomyelitic lesions of the brain. Such lesions seldom affect the pyramidal tracts alone. Even in the so-called "pure hemiplegia" of a thrombosis of the lenticulostriate arteries, some residuum of mental symptoms is the rule rather than the exception. Oblique and bizarre disturbances of gait are not unusual in hysterical patients or in those of the schizophrenic groups. The foot-slapping, wide-based gait of the tabetic patient is not often seen now, but it may be a clue to an associated taboparesis. The mincing, painful weakness of gait in a patient suffering from a multiple neuropathy may be a living historical record of the effects upon his peripheral nerves of an exogenous toxin such as alcohol. Such a toxin may affect the nerve cells of the brain as well as the peripheral nerves.

Facial Expression

The facial expressions of men have long been a subject of intense interest not alone to physicians, but also to artists, novelists, and others. With varying degrees of accuracy, one instinctively judges the mood of a person by his facial expression. Many series of scientific examinations have failed to demonstrate the validity of these judgments when they are based on still or moving photographs of the face alone. It would seem very likely that one depends upon many associated phenomena such as body attitude, speech, gait, and the environmental content for one's appraisal of the significance of a facial expression. This should not prevent the physician from noting (in writing or otherwise) the impression he gains from the facial expression of his patient. No other portion of the muscular system is apt to be so responsive to mood changes as the group of facial muscles innervated by the seventh pair of cranial nerves. Many bizarre expressions outside the range of intuitive appraisal may be seen in schizophrenic patients. Patients hearing voices inaudible to others often listen with an expression of rapt attention. The facial expression and its changes have been an important clue to correct diagnosis in some cases of "pseudobulbar palsy," in which lightning-fast changes of expression to unmotivated laughing or crying, or a queer combination of both, may occur quite involuntarily. This sign of "involuntary emotionalism" is most often seen in patients having bilateral brain lesions either of cerebrovascular disease or of multiple sclerosis. Of especial diagnostic value is the peculiar repose and unresponsiveness of the facial expression of patients suffering from a dementia or a toxic psychosis. The "stupid expression" of the Mongolian idiot is the paradigm of all stupidity while the alert, intelligent, mobile face of the brilliant young student is in direct contrast. The aloof sneer of some schizophrenic patients is very difficult of exact interpretation, but it leaves no doubt of the loathing for the practical and mundane which the patient feels.

Beyond all these more obvious and conventional variations of facial expression, there are the subtle and more delicately modulated plays of the facial muscles which depend for their interpretation upon the particular stimulus, and on all the intuitive and objective evidence the physician can gather from a patient. The intriguing and mysterious smile of the Mona Lisa has defied its audience for generations, probably because of the lack of knowledge of the environmental setting. Anatomically Mona Lisa is smiling with only one side of her face, psychologically one can only guess

at what succession of neurologic events brought about her peculiar, one-sided, "enigmatic" smile. Pallor or flushing of the skin of the face in response to some remark or circumstance are autonomic nervous system responses which also may aid the physician in interpreting facial expressions. Patients may also diagnose their doctors by the facial expression of the latter, and the wise psychiatrist avoids guiding the patient with his own facial expressions. This may be accomplished either by assuming a blank and noncommittal expression, or by removing his face from the patient's range of vision as in some variant of the passive (couch) technic.

Hands

Next to the face, the hands of many people are their most expressive body parts. It is facetiously said that neither Spanish nor Italian can be spoken correctly without the corresponding hand gestures. Beyond these cultural characteristics of a community there are the individual differences in the use of the hands as one distinctive mode of expression. The peculiarly helpless fluttering which is associated with feminine dependence, and the clenched fist symbolizing the aggressive powerfulness of the male are two of the more standardized types of expression in Anglo-Saxon communities. The restless hands of table top drummers and "doodlers" may be part of the tenseness of an anxiety syndrome. The Hindus and others in their ritual dances and ceremonies have elaborate stereotyped meanings for various hand positions and such racial stereotypy has a counterpart in the individual stereotypies of the mentally ill. In general the use of the hands as organs of expression is more subject to voluntary modification than is the facial expression, and these motions are not so susceptible of direct or easy interpretation.

Voice

Of all the means of expression, the voice is perhaps the most significant medium, not alone as a carrier of definite, logical words, but also as a method of expressing feeling and emotion The purely static physical characteristics of voice sounds such as timbre, pitch, and loudness do not alone comprise the means by which this expression is accomplished, but it is these characteristics which, together with the succession of modified sounds and accents, impart the meaning to the spoken word which is lacking in the written word. As a result of the generally mediocre acting on the cinema screen and in other mediums of entertainment, the general public has a stereotyped idea of the appropriate voice for expressing grief, joy, or the other emotions. Unfortunately, people in real life are seldom possessed of these standardized means of expression even though they may imitate them, but much intuitive information may be gained by the doctor by listening to the sound as well as to the words of a patient's speech. Many depressed patients speak in a low, weary, monotonous tone which seems symbolic of the dreariness and hopelessness they feel in living. In the anxiety states, and in the anxious syndromes often seen early in schizo

tract lesions may give an important lead to the diagnosis of vascular, degenerative, or encephalomyelitic lesions of the brain. Such lesions seldom affect the pyramidal tracts alone. Even in the so-called "pure hemiplegia" of a thrombosis of the lenticulostriate arteries, some residuum of mental symptoms is the rule rather than the exception. Oblique and bizarre disturbances of gait are not unusual in hysterical patients or in those of the schizophrenic groups. The foot-slapping, wide-based gait of the tabetic patient is not often seen now, but it may be a clue to an associated taboparesis. The mincing, painful weakness of gait in a patient suffering from a multiple neuropathy may be a living historical record of the effects upon his peripheral nerves of an exogenous toxin such as alcohol. Such a toxin may affect the nerve cells of the brain as well as the peripheral nerves.

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rapid and of small excursion. They tend to increase under stress and during activity. At times they may be so marked as to constitute a chief complaint. The tremors of hyperthyroidism are of much the same type and are influenced by stress and activity in the same way The tremors of paresis may be very rapid also, but they usually tend to be coarser and to affect the lips and tongue as well as the hands. In multiple sclerosis the tremor is most pronounced when the muscle groups responsible for the tremor are bringing a movement to a precise termination, as in touching the tip of the nose with the index finger. This same type of tremor may be seen in many diseases of the nervous system in which there is a pyramidal tract lesion.

The foregoing tremors affect chiefly the fingers and hands. The "pill rolling" tremors of diseases of the lenticulostriate nuclei, such as paralysis agitans and hepatolenticular disease, are described typically by the hands, but the same basic tremor mechanisms may affect any voluntary muscle group. These striatal types are apt to be coarse and slower than any other type of tremor and, when typical, may be quite diagnostic in themselves Many of them cease during at least part of a voluntary movement Diseases of the striatal and allied systems may be due to a variety of agents in addition to inflammatory and degenerative disease. Among these agents are exogenous toxins such as mercury, manganese, and carbon monoxide. The tremor of senility is probably compounded of the weakness of pyramidal tract disease and the tremors of vascular disease of the striate bodies One type of tremor is of particular interest to the psychiatrically minded doctor and this is found in delirium tremens. It is usually a coarse, persistent tremor, difficult of description but in most cases pathognomonic of the disease at first glance.

Tics

Tic-like contractions of muscles producing sharp irregularly recurring movements of the face or limbs are seen in a variety of psychiatric patients In some instances tics of the face may be found to be associated with paresis, but this occurs only in the minority of cases. Some patients who have suffered from tics for years have been shown at postmortem examination to have a lesion of the striate bodies of the cerebral hemispheres. Certainly many, if not most, patients with tics and tic-like movements have no demonstrable pathologic lesion in association with them Many case reports in the psychiatric literature have given extensive analyses of the psychologic origin and symbolism of the tics found in individual patients. In general those discussions show the tics as a behavioristic partial expression of a complete movement, which would normally be used to express the emotional conflict if the movement were completed In actual practice, the obvious tic of the face, neck, or shoulders is very difficult to evaluate either from the standpoint of somatic pathology or psychopathology. The involuntary tics of the facial muscles seen in tic douloureux* are really reflex responses to sensations of stabbing pain in the face. They are rarely associated directly with any psychiatric syndrome In the young, sharp movements of the distal portions of the extremities, irregularly timed, may be symptomatic of Sydenham's chorea, a disease which may be of infectious

* Tic douloureux, or trifacial neuralgia, is not a muscular tic at all, but derives the name from the spasmodic contractions of the facial muscles which result from the excruciating stabs of pain in the face

tains may in the end be of more practical value to him than many a time-consuming objective observation. Both are important and neither should be overlooked. In the senile and some other states, an indecisive querulousness often reminds the physician that the chief concern of the patient is irritation with the more petty arrangements of living rather than life in its larger aspects. Patients with demonstrable brain lesions often have characteristic voice changes. The measured monotony of the postencephalitic patient, the flatness of speech of the patient with multiple sclerosis, and the tremulous difficulties with R's and S's of the paretic are examples of these.

Intuitive Deductions

General appearance, attitude, gait, facial expression, hands, and voice are the important component parts of expression, and all these add up to a whole that is more than the sum of these parts. The countless combinations and permutations that are possible make up an infinite variety of expressions, each one of which is unique. It is perhaps more of an art than a science to evaluate the things these various modes of expression are trying to say, but it is an art possible of acquisition and training. Except in very rare cases, all the wholely objective information that can possibly be obtained concerning a patient will not alone suffice to form the basis for a proper diagnosis. To fill this hiatus the information the doctor's intuition gives him must be considered, too. This situation is not unique in psychiatry, but also prevails in scientific research, where the successful venture into a territory which was previously uncharted is directed, more often than not, at least partly by the dictates of the scientist's intuition. Perhaps intuition is the product of an unconscious assimilation of previous experience, but it has the advantage of being free of the factual distortion to which our usually incomplete logic often subjects our conscious thinking It is unwise to depend wholely upon intuition in psychiatry, but it is equally unwise to disregard it.

NEUROLOGIC EXAMINATION

Many psychiatric symptoms are the result of "organic" changes in the function of the central nervous system. These symptoms are due to interference at the highest levels of integration and complexity of which the central nervous system is capable. There may be important associated clues as to the nature of the illness when the less highly integrated functions of the nervous system, such as simple reflexes, are carefully examined. The finding of parallel disturbances of the functions of the central nervous system at both high and lower levels of integrative complexity, often furnishes important diagnostic clues. Only such portions of the usual neurologic maneuvers as may yield such information are considered below. Chapter XVIII in this book will give more comprehensive information.

Tremors

In addition to the gait and station and general attitude of the patient, the presence of tremors is important. Most tremors in psychiatric patients exist without demonstrable pathologic basis, and they are found principally in association with the agitated and anxiety states. To many people "nervousness" is synonymous with "shakiness." These tremors are apt to be

simultaneous convulsive seizure; longer runs are more apt to be associated with a convulsive seizure. Short runs of aberrant configurations have been found in the records taken from people who never have and who never do develop convulsive disorders which can be recognized clinically.

The significance of these short runs of changed and aberrant electrical activity of the brain is an interesting subject for speculation. They may very well represent a change of brain physiology which profoundly affects the continuity of such functions as consciousness and consecutive thinking. Since each run may occupy anything from a fraction of a second to several seconds, it would be difficult to secure direct evidence on this point, for the duration may be too short for clinical findings. The longer runs of aberrant activity are almost always associated with such a break in continuity of consciousness and this is easily observed externally because of the longer time intervals. Perhaps these rapid fluctuations are indications of fluctuations in brain function upon which depend the modes of behavior and thinking which constitute the mental syndromes of epilepsy. More obvious breaks in the continuity of consciousness and other functions occur in such related syndromes as petit mal, the "psychomotor equivalents," epileptic automatism, and the epileptic furor.

Convulsive disease in association with more or less obvious anatomic lesions of the brain may also demonstrate electroencephalographic changes, as well as chemical, neurologic, and roentgen ray findings Only one of these diseases is commonly associated with mental syndromes and that is paresis. Any convulsive disorder occurring for the first time in middle age or later should be considered paretic on a statistical basis until this diagnosis can be disproved. Paresis is not as frequent as it used to be, but untreated paresis is just as fatal today as it ever was. Convulsive disturbances may be the first clinical evidence of paresis, and usually such patients recover under prompt and adequate therapy. Most untreated paretics will have convulsive symptoms at some time during the course of their disease. The convulsions may be generalized or localized to one or more muscle groups They may or may not be accompanied by unconsciousness; the localized or Jacksonian types are generally not A paretic may die in a status epilepticus, although a localized convulsive movement may persist for days without endangering the life of the patient

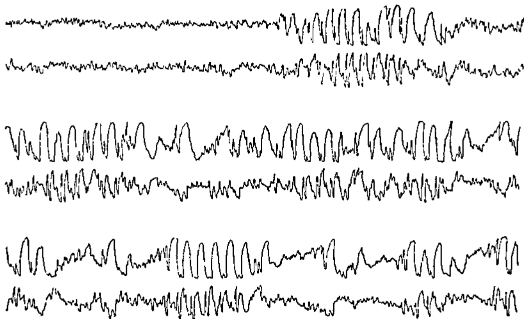
Eyes

The eyes and the nerves associated with their function may furnish important contributory information in many psychiatric patients. The pupillary reflexes are usually tested in two ways—for the reaction to light and for accommodation. Each is tested separately. To determine the reaction of the pupils to light stimulation of the retina, the patient may be directed to look steadily at any object in the room at some distance. A bright beam from a flashlight may then be directed from the side (to avoid having the patient involuntarily focus on the light and thus bring into play his accommodation reflexes of pupilloconstriction) and the pupillary responses of that eye and the contralateral eye noted. The procedure should be repeated on the other side The room ought to be dark enough so that the patient's pupils are moderately dilated at the onset as an initially contracted pupil cannot contract very much more in response to light. To test the pupillary response to accommodation the patient may be requested

or psychologic origin. In any case, it has important psychiatric components. Sharp tic-like movements of large muscle groups are seen in the familial disease of Huntington's chorea.

Convulsions

The most frequent variety of generalized convulsive seizures are those which begin early in life and occur at intervals throughout the lifetime of a patient. They are almost always accompanied by unconsciousness. These patients are referred to as "idiopathic" epileptics to point out the fact that the cause of the fits is unknown. At least half of these patients have some type of mental syndrome at some stage of their disease, and in some few cases there may be a major psychosis which is long lasting. It seems evident that some degree of pathologic change occurs in the brain structure of



Fi[illegible]
The [illegible]
who [illegible]
his first known convulsive seizure

many of these patients, but it is not clear whether the coexisting mental syndromes are the consequence of these changes, or are a psychologic reaction to a disease the manifestations of which may strike without warning anywhere, anytime, or whether they may be some parallel disturbance of brain function. A very interesting insight into the disturbed physiologic activity of the brain of many idiopathic epileptics is provided by the electroencephalogram. Figure 601 is a record of dysrhythmic activity such as is frequently found in the epileptiform disorders. Other types of unusual configuration occur in the records of most epileptics, and whatever the ultimate interpretation of these changes may be, they indicate that the functions of the brain in most of these patients differs from those of others. Short runs of the typical "spike and dome" or other aberrant configuration, may be seen frequently in these records without any external evidence of a

of the doctor they will both see the moving finger simultaneously for each axis. These examinations or more
quently during the treatment of a
cases of intracranial mass lesions. . . .
field suggesting uniocular disturbance (prechiasmal syndrome or monocular blindness), inability to see laterally into either temporal field (chiasmal syndrome or bitemporal hemianopsia), or inability of both eyes to see well to one side (postchiasmal syndrome or homonymous hemianopsia). Some acutely disturbed patients may show a field of vision which is markedly narrowed concentrically in each eye. This "tunnel" vision is seen chiefly in patients having hysterical disturbances of other sorts, such as anesthesias or paralyses, but tunnel vision does occur in somatic ocular disease such as retinitis pigmentosa.

The muscles which move the eyes and elevate the upper eyelids are innervated by the oculomotor and trochlear nerves which have their nuclei of origin near the cerebral aqueduct in the midbrain and by the abducens. The orbicularis oculi closes the eyelids over the eye and is innervated in common with other facial muscles of expression by the facial nerve. These orbicularis oculi muscles serve in part as molders and sculptors of the upper part of the face. They narrow with suspicion, they widen with surprise and pleasure, and they etch "crow's feet" into the upper cheeks of the man who has enjoyed a good joke all his life In hemiplegic syndromes the palpebral fissure on the affected side is a little larger because of the weakness of the orbicularis. The anxious stare of protruding eyeballs in hyperthyroidism can scarcely be overlooked.

The movement of the eyeball itself can be tested by having the eyes follow together and separately the examiner's moving finger which travels from one side to the other and up and down. Obvious lack of parallelism of the visual axes of the two eyes may be a contributory factor in the production of some psychiatric impressions their "crossed" eyes may create in others. Sometimes isolated paralyses of one or two of the extraocular muscles may be the only objective evidence of an encephalitis which has involved the nuclear structures about the cerebral aqueduct in addition to other areas of the brain and brain stem.

The motility of the eyeballs is easily observed. Movement is apt to be slight in paralysis agitans and in catatonics. The eyeballs may rove from side to side aimlessly in the dementias and in the arteriosclerotics. Eyes may be evasive in the depressed or ill at ease, or they may be forced into the semblance of frankness in the case of the chronic liar. An unrecognizing, wandering gaze may be a sign of confusion, disorientation, or lack of comprehension. The movements of the eyes together with facial expression tell the experienced doctor much about the patient that would be difficult to learn in any other way.

The oblique eyes and epicanthal folds of the Mongolian idiot are readily recognized when typical, but most cases of Mongolian idiocy have incomplete versions of this syndrome.

Face

Sensation about the face and a large area of the scalp is mediated by the trigeminal nerve. Many lesions of neurologic interest affect the ability to perceive facial stimuli, but few of these are directly connected with any

to follow the examiner's finger as it travels from a distance of three feet in front of the patient to his nose in one to three seconds. The narrowing of the pupillary apertures may then be seen. Inspection of the pupillary edge for coarse irregularities should be made.

Contraction of the pupil is accomplished by the circular muscle fibers of the iris which receive innervation from the oculomotor nerve. Dilation of the pupil is accomplished by the radial muscle fibers which are innervated through the cervical sympathetic nerve complex. Contracted pupils are found in patients who have taken sizable doses of opiates or other sedatives, and they do not dilate very much when the light is dimmed. Dilated pupils may be found in many psychiatric states of anxiety, fright, or schizoid psychosis. Markedly dilated, fixed pupils are usually due to the use of atropine or its analogues during a previous eye examination. Contracted pupils with grossly irregular, unequal outlines, which do not react to light but do react to accommodation, show the classical eye signs of neurosyphilis, but most syphilitic patients having pupillary signs present an incomplete version of this Argyll Robertson pupil. The location of the lesion responsible for this syndrome is unknown. A confusing syndrome of no known pathologic significance is the Adie syndrome. It consists of unequal pupils which do not react to light. The larger pupil is referred to as being tonic and frequently the quadriceps reflexes are absent presenting a picture which might be confused with tabes dorsalis superficially.

The use of the ophthalmoscope is an important adjunct to the psychiatric examination, for in looking at the ocular fundus one is virtually looking at a sample of the surface of the cerebral cortex. The state of the arteries of the fundus is a particularly good index of the presence or absence of vascular disease of the cerebral cortex in older patients. The pupils may be opened by a mydriatic to make the examination easier, but this is usually not necessary unless one wishes to visualize the macula region. The appearance of the optic disk should always be noted, particularly for evidence of optic nerve atrophy or papilledema. In younger patients with evidence of mental deficiency it may be well to look at the macula region for the "cherry red spot" which is diagnostic of some of the degenerative brain diseases such as amaurotic familial idiocy. Often, as in Schilder's disease, it is important to know that the amaurosis is *not* due to optic atrophy.

The visual field examination must be done in some special situations in psychiatric practice, and should be done in many patients. It is less time-consuming to do a rough visual field examination than to describe the technic of doing it. The rough visual field examination* is essentially a matching of the presumably normal visual fields of the examiner with those of the patient. The doctor and patient may stand about three or four feet apart facing each other. The examiner has the patient close one eye (say his right) and closes his own left. They then look steadily at each other's remaining open eye. The examiner can easily see that the patient focuses on his own pupil and he does the same with the patient's pupil. The examiner slowly brings his finger in from the periphery toward the zone of central vision, carefully keeping his finger in a plane midway between him and the patient. This is done from each side, and from top and bottom for each eye. The patient is instructed to say when he first sees the finger moving in from the periphery. If his visual fields are the same as those

* Sometimes called the "confrontation test"

degree of mental stability he has. The chief difficulty most otologists have with their hard of hearing patients is helping them develop more useful attitudes toward taking their place in the world.

One of the most frequent complaints any doctor hears from the patients who come to him is that of "dizziness." It is a word which means many things to different persons. In only a small minority of these patients do the vestibular tests, involving reactions to turning, changing temperatures in the external auditory canal, or electrical stimuli in the canal, show any evidence of either a peripheral or central lesion of the vestibular apparatus. On the other hand, many patients with normal vestibular tests who complain of "dizziness" have no psychiatric difficulties Many other etiologic agents enter into consideration. These include exogenous toxins such as caffeine and tobacco, endogenous toxins such as found in metabolic diseases and distant infections, and vascular disease of the brain. Barring all these agents there still remains a considerable group of patients with normal vestibular tests who complain of "dizziness" and in whom the complaint is a part of a psychiatric syndrome

Mouth and Tongue

There are few obvious or marked anesthesias or paralyses of the mouth or tongue that have direct connection with psychiatric disorder. Such complaints as dryness of the mouth and peculiar sensations are very frequent neurotic complaints. Some of the complaints of dryness may be the result of decreased secretion from the salivary glands because of disturbed autonomic balance in which the parasympathetic secretory functions are held in abeyance. The autonomic balance between the sympathetic and the parasympathetic elements is frequently disturbed in psychiatric syndromes, especially in the anxiety states. Therefore it is reasonable to expect that some of this disturbance will be manifest externally in such symptoms as dryness of the mouth. On the other hand, pleasurable anticipation of good food or company or sexual opportunity is very apt to be associated with excessive salivation or even drooling. Complaints of peculiar tastes and sensations are met with in all sorts of psychiatric patients Auras of oncoming epileptiform attacks are frequently referred to the mouth, and sensations of bad tastes or licking of the lips may be the signals heralding a convulsive seizure. The protruding large tongue of the Mongolian idiot is easily recognized by its association with the "stupid" expression

Larynx and Muscles of the Neck

The motor innervation of the larynx is by way of the laryngeal branches of the vagus nerves, while the sternocleidomastoid and trapezius muscles are innervated by the spinal accessory nerves Several types of laryngeal disorder are found in the psychiatric syndromes. A suddenly appearing aphonia without other signs is usually an hysterical aphonia This tends to subside spontaneously. The peculiar sensation of the unswallowable "lump in the throat" or "globus hystericus" is seen often in acute anxiety. Frequent coughing and "clearing of the throat" may be a habit spasm or tic which has developed as part of a neurotic or psychotic disorder. Involuntary head nodding is usually in the horizontal or "no" plane and less frequently in the vertical or "yes" plane Probably a large proportion of older individuals suffering from involuntary head nodding have no psychiatric condition as

psychiatric syndrome. Not uncommonly syphilitic neuritis of the fifth nerve may produce a painful anesthesia of the face, but ascertaining the presence of syphilis in psychiatric syndromes is not difficult in most instances. There are many types of painful syndromes about the face which simulate tic douloureux. Some of these imitations are part and parcel of an anxiety conversion syndrome in which surgical section of the fifth nerve or its root seldom produces lasting beneficial effects. The best treatment in these cases is psychotherapy of the individual possessed of the syndrome.

The muscles of the face are all innervated by the facial nerve, except for the muscles of mastication which receive their motor impulses from the masticator nerve (a part of the fifth pair of cranial nerves) and the elevators of the upper lid. There are few paralyses of the facial muscles which are directly connected with psychiatric disease. Paralyses due to lesions of the seventh nerve itself are usually very marked and involve the brow; those of more central origin are usually milder and spare the brow.

Ears

The sensory supply to the skin of the outer portion of the external ear canal is by way of the vagus nerve, but the great nerves of hearing and vestibular sense are the auditory and vestibular divisions of the eighth pair of cranial nerves. Gross disturbances of hearing are best determined by audiometric tests which can be so applied as to distinguish between the defects due to faulty conduction of or faulty perception of sound waves Hearing tests usually center about a calibrated instrument producing test sounds. The audiometer is such an instrument which produces sounds of measured pitch (frequency) and intensity (loudness) for the testing of hearing. Most of the psychiatric syndromes in which disturbances of hearing exist are of the central group. One very interesting auditory symptom is hyperacusis or superacute hearing. It occurs frequently in the degenerative brain diseases of the amaurotic familial idiocy group and also very remarkably in the manic phase of manic-depressive disease. The infant with amaurotic family idiocy is very docile and quiet except in his startling reaction to sudden loud sounds. The manic patient hears and repeats whispers at a distance which would make his hearing seem incredibly acute for a well person. In neither of these two situations is the mechanism of hyperacusis very well understood. In the manic patient it may be that the threshold for hearing is not really reduced, but that the reflex pathways of hearing facilitate the responses to what is heard. Some experimental drugs of the amphetamine group have a similar effect, but their therapeutic use in the deaf is not advocated because of toxic side reactions.

The psychologic reaction to decreased hearing caused by some lesion of the ears or of the auditory nerve has been a subject of interest to psychiatrists for a long time. The individual who does not hear well is particularly prone to translate his own feelings of personal inadequacy and guilt into a suspicion that the conversation which he cannot quite hear contains criticisms of him, or even plots against him. Suspiciousness and paranoid ideas are not the only types of mental symptoms seen in the hard of hearing. There are many among them who shrink from contacts with the impatient world that is critical of the sight of a hearing aid. There are undoubtedly social penalties for any physical defect and how adequately a disabled person may cope with them depends largely upon the

extremities tends to diminish in acuteness with age, and its bilateral absence in persons past forty need not be remarkable.

Reflex Examination

The reflexes usually tested in the course of an examination are often separated into the superficial and deep groups The superficial reflexes are many and among these there are only a small number which are of proven clinical usefulness. The Chvostek sign (tapping over the facial nerve in the preauricular region to determine a fibrillary response of the facial muscles) is often found in states of increased irritability, such as in the low blood calcium stage of parathyroid hormone deficiency. Some of the anxious people met with in practice may show positive Chvostek signs without a corresponding low blood calcium level, and the sign may also be present as an isolated phenomenon in healthy persons. The abdominal reflexes are usually absent early in the course of multiple sclerosis, and they tend to diminish on the side of a pyramidal tract lesion. Bilateral absence of these reflexes in older people, especially in mothers, is of no significance. The responses to plantar stimulation (the Babinski technic) or some substitute (such as the Gordon, Chaddock, or Rossolimo technic) may give information as to the functional state of the pyramidal tracts. The abnormal responses to this type of manipulation are prompt dorsiflexion of the great toe and spreading of the other toes From the practical standpoint a considerable amount of neurologic experience is necessary for the correct interpretation of these responses. Abnormal responses may be found in conditions permanently affecting the pyramidal tract such as brain tumors, encephalitides, cerebrovascular disease, multiple sclerosis, and severe degenerative brain disease. Less permanent conditions causing temporary interruption of the activity of the pyramidal tracts may also give rise to abnormal response to plantar stimulation. These include diabetic coma, the post-epileptic states, narcosis, and toxemias For the purpose of examining a psychiatric patient, no more searching inquiry into the superficial reflexes than that outlined above may be necessary.

The deep reflexes* are the chains of events set into motion by a more or less standardized stimulation of the tendon or periosteal receptor nerve end organs. The reflexes of this group generally examined are the biceps and triceps reflexes of the arm, and the knee and ankle tendon reflexes of the leg. These are symmetrically and bilaterally increased in the anxiety states, in many of the psychoses, especially in the catatonias, in encephalitis, paresis, cerebrovascular disease, and in some of the toxemias. Unilateral increase of tendon reflexes may be seen in unilateral pyramidal tract syndromes † Deep reflexes tend to diminish or become absent in peripheral nerve disease and in the legs in tabes dorsalis.

Accessory Neurologic Features

The neurologic examination is not merely a collection of stereotyped tests. Many other features add to and complement these specific tests. The neurogenic arthropathies such as the Charcot joint, or the trophic disease of the skin of neurogenic origin, may, in individual cases, be of considerable

* The deep reflexes are really clinical demonstrations of the tendon stretch reflexes and their disturbances

† In experimental pure pyramidal tract lesions in primates, the tendon reflexes are hypoactive and there is decreased muscle tone.

the basis. Some carefully studied patients have had vascular lesions of the basal nuclei of the brain which may have been responsible. Many operations have been performed upon the peripheral nerves or muscles of the neck on some of these patients, but an operative cure of spasmodic torticollis is rare.

Sensory Examination

Few patients ever have a comprehensive study made of the competence of their sensory apparatus, for such extensive studies are time-consuming and seldom valuable except in selected cases of organic disease of the nervous system. Testing pain sensation by the perception of a pin prick need not take much time, and the test should not be omitted, for often an anesthesia of the hysterical type may quickly be recognized. These anesthesias are not anatomic in their distribution, except perhaps in doctors or anatomists who become patients. They may correspond in distribution to the areas which might be covered by gloves or stockings, or in hysterical hemianesthesia they may extend right up to the midline, instead of falling just short of it as in the anatomic hemianesthesias. Insensitiveness may shift from one area to another with suggestion, or show other incongruities indicating its true nature. The hysterical anesthesia usually serves a psychologic purpose, however ill-advised that purpose may be, and the apparent purposefulness of the symptom is one of the trademarks by which it may be recognized. The areas of anesthesia which may occur in peripheral neuropathies may superficially resemble some of those found in the hysterias, but other associated neurologic signs will enable one to evaluate them properly. Thermal sense may also be tested as part of the sensory examination.

Complaints of odd sensations such as "crawling" sensations, intractable itching and burning may be present. By no means all of these are of psychiatric origin. Sometimes no cause and little relief can be found, but these medical failures are not in themselves proof of the psychiatric origin of the symptoms. A great many guesses have been ventured by dermatologists and others as to the nature of these conditions, but no uniformity of opinion exists. There are doubtless many facts concerning the physiology of the skin and its sensations yet to be discovered, and some of these may throw light on the nature of many mystifying cases of pruritus and neurodermatitis. There is, however, a definite group of patients, largely suffering from anxiety syndromes, in whom psychiatric attention is rewarded by a subsidence of these subjective sensory symptoms as well as the observable lesions of the skin.

The sense of position is easily tested by having the patient close his eyes while his finger or toe is passively moved back and forth. An alert individual with an intact nervous system can promptly identify the position of the digit in question. Sense of position can also be tested by having the patient actively perform simple movements with his eyes closed. Touching his index finger to the tip of his nose or touching one knee with the heel of the other foot are acts frequently used in these tests. Sense of position may be impaired in the peripheral neuropathies, in tabes dorsalis, in syringomyelia, in avitaminosis, and in many other conditions. Vibratory sense closely parallels sense of position since both modalities of sensation are mediated by nearly the same neural pathways. Vibratory sense of the lower

When phenobarbital is used in the treatment of chorea in children (especially in association with typhoid vaccine fever therapy) a measles-like rash may appear, but it quickly disappears on the cessation of therapy. Mesantoin, tridione, and dilantin may all cause skin lesions.

The skin and scalp of some psychiatric patients may show the effects of neglect either in lack of cleanliness or some other feature consequent upon it. Lice of various types, skin infections and dermatoses may often be seen in neglected psychotic or psychopathic patients. The scars of a hypodermic needle on the skin may suggest evidence of narcotic addiction. Sometimes these needle marks are found in the form of a "V" about the antecubital vein of such a patient and indicate that the addict has taken his morphine or heroin by the intravenous route Bruises or lacerations may be mute evidence of attempts at self mutilation or destruction Thinned eyebrows may be the result of plucking or they may be an early sign of leprosy with its associated neuropsychiatric symptoms.

Head

The head should be palpated for any unusual configurations or bilateral asymmetries that may be present. Exostoses of the external table of the skull are often associated with underlying meningiomas Odd skull configurations direct attention to the possibility of an intracranial space-taking lesion especially in children The skull should be lightly percussed to determine any unusual percussion note or points of tenderness. The configuration of the face and its expression has been discussed earlier in this chapter. In any patient with a history of cranial trauma it is well to look for palpable bony evidence of the trauma

Mouth

The mouth often gives hints as to the habits of a patient Obviously well cared for teeth suggest that a certain amount of interest in the world and its affairs prompted the care. On the other hand, dirty, neglected teeth may often be found in the dejected, and in individuals whose mental images do not include a realistic appreciation of the healthy body. That is often the case in the schizoid patient and in the elderly psychotic patient. Tobacco stains on the teeth give some quantitative appreciation of the amount of tobacco used. The permanent teeth of the congenital syphilitic may be peg shaped and the upper central incisors notched (Hutchinson's teeth). The gums in lead poisoning may show the bluish discoloration which arouse suspicion as to the presence of a saturnine (lead) encephalopathy. Dull, purplish, hypertrophied gums may result from overzealous administration of dilantin for the control of epilepsy The casual examination will seldom be sufficient to evaluate critically the presence of infection in or about the dental structures, but such an examination may suggest reference to a dentist. The same is true for the lymphoid structures of the tonsillar fossa and pharynx as well as the sinuses, where the services of a laryngologist may be necessary Psychiatric thought has followed the pendulum of medicine in general in swinging from overemphasis to underemphasis on the question of "focal infection " There is no question that a few psychiatric patients have had mental difficulties due to such a focus of infection, because their mental symptoms leave them when such an infected area is

importance when examining the patient. The specific tests usually enumerated in a neurologic examination are clinical evidence of health or disease at the very lowest levels of organization of the nervous system that such testing can appraise. For instance, an intact knee jerk is presumptive evidence that the reflex pathway consisting of tendon end organs in the quadriceps tendon, the femoral nerve, the anterior primary divisions of the lumbar third and fourth spinal nerves, the corresponding dorsal spinal roots, the spinal cord at the same level, and anterior spinal roots of the same, the quadriceps femoris motor end plates, and the quadriceps muscle are all anatomically and functionally intact as far as this one reflex is concerned. When a similar analysis is assembled for all of the various neurologic tests a great many useful facts become known concerning the health of the nervous system, but all these facts together do not constitute more than a very small fraction of what goes on in the living, functioning nervous system, for only the very lowest levels of nervous activity can be tested clinically in a direct and objective fashion. The function of the intermediate and higher levels of organization of the nervous system must be inferred from the psychiatric studies. However, such examinations as those just described may quickly inform the doctor that he is dealing with a patient with a gross anatomic lesion, such as multiple sclerosis or paresis, rather than an anxiety state. The therapeutic importance of such a distinction is obvious.

Skin

The skin is subject to some characteristic and a few less specific changes in patients with psychiatric disorders. One of the most characteristic of lesions is the sebaceous adenoma of the cheeks in some cases of tuberous sclerosis. These adenomas are arranged in a "butterfly wing pattern" on each side of the nose, and are signs of coexisting multiple tumors of the brain of a mixed glioblast-neuroblast type. There may also be an associated hypernephroma of the kidney or perhaps a rhabdomyoma of the heart. The sebaceous adenomas (or cysts) often do not appear before puberty, although the associated mental deficiency does. This disease is not common.

Dark, thickened, scaly lesions symmetrically placed on the exposed extensor surfaces of the skin may be a significant indication that the nervous system, too, is suffering from a lesion of pellagra. Since the mental symptoms of pellagra are quite varied, the discovery of characteristic skin lesions is an important diagnostic finding. Malignant disease of the skin or its appendage, the breast, may introduce the possibility of metastatic lesions of the brain into consideration. Excoriations of the skin, with or without pruritus, may be found in a wide variety of psychiatric patients. Occasionally malingerers excoriate their skin deliberately in order to carry some cherished point.

Various types of skin eruptions caused by drugs used by psychiatric patients may cause considerable trouble in diagnosis. The bromide rash may occur in those using bromide as a sedative for a long time. Its diagnosis may be confirmed by the history of bromide medication and by a blood bromide determination. It disappears when the blood and tissue bromides are replaced by chlorides. Exfoliative dermatitis is a dreaded complication of arsenic and other drug therapy which may arise any time to confront the doctor treating a patient with tryparsamide for paresis.

neurotic patients have low basal metabolic rates entirely unconnected with thyroid disturbances. In these patients thyroid extract or thyroxine in large amounts for a long time usually does not change the metabolic rate or produce any other desired effect.

Chest

General practitioners have many considerable advantages in the examination of the psychiatric patient. One of these is the experience they have had in the examination of patients for visceral disease. Malignant disease of the lungs has a high incidence of metastases to the brain; tumors of the mediastinum metastasize less frequently. According to a number of sound psychiatric observers, bronchial asthma is in many cases a symptom of emotional disturbance, and these doctors have reported remissions and cures of asthma under psychotherapy. The peculiar euphoria of patients with low-grade febrile pulmonary tuberculosis is proverbial. This is very likely a non-specific sort of reaction to continued low-grade fever. The character of the breathing in the anxiety states is a very interesting point to watch Studies of breathing in neurotic people have shown an irregularity which is claimed to be almost pathognomonic of anxiety. Occasionally hyperventilation, particularly under stress, may cause variations in the mental state by means of the relative blood alkalosis which is produced

The examination of the heart has enough importance in psychiatric patients never to be omitted. The various tachycardias, paroxysmal or otherwise, all have the possibility of being associated with some mental syndrome. This is another situation in which the pendulum has swung back and forth a good many times, but somewhere near the neutral position lies the truth.

[illegible]

The differentiation is often most difficult. It may often be made by pulse and basal metabolic rate estimations under pentothal narcosis.

Early in the course of subacute bacterial endocarditis the mental symptoms may overshadow others in their magnitude Postmortem examination of the brain in such patients reveals a marked amount of vascular intimal reaction and it is possible that this and the continued fever produce changes in the function of the brain cells to account for the mental changes. The most constant mental symptom is irritability The majority of the pitifully few patients* who have recovered from this disease have no residuum of mental symptoms.

The problem of the patient with precordial and substernal pain who does not have any physical or laboratory findings is a very difficult one, and often requires the collaboration of a cardiologist and a psychiatrist for solution. The general practitioner who is well versed in both fields holds an advantageous position in this respect. It has long been suspected that the arteriosclerotic, hypertensive patient with a lifelong history of tension does not usually become free of mental symptoms when angina appears. In fact his anxieties are often augmented, particularly when the substernal pain is mild. Patients of this sort who have died from some other disease have often shown perfectly normal hearts on autopsy examination It might be postu-

* The recent use of penicillin with or without heparin has brightened the outlook considerably and reduced the mortality to about 20 per cent.

properly treated. A somewhat greater number of patients seem to be benefited by treatment aimed at minimizing such infection. In any case, it does no harm to put a patient who is very ill mentally in the best possible physical condition. In common with all physicians, however, those practicing psychiatry do not wish to be the cause of unnecessary surgical procedures.

The tongue and lips may give some information in patients with vitamin deficiencies which not infrequently coexist with severe mental illness. Sometimes the vitamin deficiency appears to be the cause of the mental illness as in pellagra, sometimes it seems to be the consequence of the psychiatric disorder as in the catatonic patient who has refused food for a long time, or the neurotic woman whose attempts at slenderizing have succeeded well but not wisely. Older people seem prone to develop the symptoms of avitaminosis more early than younger people. In states of clinical avitaminosis B there is a marked diminution in the cerebral metabolism as measured by diminished glucose utilization, and there are degenerative and vascular pathologic changes in the brain, spinal cord, and peripheral nerves.

Pellagrous glossitis and stomatitis with its swollen, reddened tongue and mucous membranes, and the oversalivation and drooling, is an impressive sight in the full-blown form Most cases of pellagra seen in private practice in the United States are less marked than those seen in clinics or by the public health nurse. Pale lips with fissures at the corners of the mouth may be the only clinical sign of ariboflavinosis, but the peculiar magenta hue of the tongue which may accompany it can be helpful in confirming this diagnosis. The importance of this condition is that it serves as a signpost pointing to the fact that the patient may have other vitamin deficiencies as well. If any of these signs are present all the vitamins should be administered in full dosage as one can treat all the avitaminoses simultaneously. The nervous system is particularly avid for the vitamins of the B group, especially thiamine, nicotinic acid, and perhaps pyridoxine.

The bitten and chapped lips of anxiety in some of the neurotic patients may add to the other evidence when the examination has been completed.

Neck

The symptoms of spasmodic torticollis are occasionally interwoven with a psychiatric disorder. The connection is never so obvious that a first-hand diagnosis may be made. Enlarged lymph nodes in the neck may partly confirm a suspicion of infection of the mouth, of the presence of syphilis, or of malignant neoplastic disease. Enlarged supraclavicular nodes may introduce the diagnostic possibility of malignant disease of the stomach or colon. Particularly in the presence of anxiety symptoms and tachycardia, the neck should be most carefully palpated for evidence of thyroid enlargement. Absence of such palpable enlargement is not a very important finding, but its presence is. No one has ever determined where the process of which hyperthyroidism is a part has its origin. Perhaps emotional disturbances precede the hypersecretion of thyroid hormone, or perhaps it is the other way around. In any case a very large percentage of hyperthyroid patients have some emotional or conative symptoms. These usually are of the nature of a confusion, depression, anxiety, or some odd mixture of psychiatric symptoms. Occasional patients exhibit emotional disturbances after long continued administration of large doses of thyroid extract. Many

who develop peptic ulcers. This was particularly true among men in the United States Army during the recent war. Under the stresses of Army life, both at home and abroad, a large number of previously unaffected men developed signs of peptic ulcer. A strikingly high percentage of them were open, frank individuals who showed a rather large amount of dependence in their characteristic life attitudes More arguments linking personality type and ulcer with mental stresses might be read into this relationship if the majority did not follow the usual rule of developing symptoms in the spring and fall. It is difficult to conceive of particular stresses of Army life which occur only in the spring and fall. The evidence connecting peptic ulcer with frank mental illness is even less impressive, as is the paucity of prompt remissions of ulcer symptoms when psychotherapy has been used without dietotherapy. All in all, there has been no incontrovertible demonstration that abnormal psychiatric states or particular personality traits may be correlated with the incidence of peptic ulcer. While the occurrence in the stomach of anatomic changes which can definitely be attributed to psychiatric disorder is rare, the symptoms of a demonstrable peptic ulcer may be aggravated by emotional stress. In the presence of emotional upsets such as may occur in the prolonged psychoneuroses, changes in the motility of the stomach are frequent, and often may be accompanied by alteration in the secretory activities as well. These respond surprisingly well to appropriate psychotherapeutic measures directed primarily toward the psychiatric situation and not toward the gastric symptoms.

The *colon* may be examined by almost direct palpation through the abdominal wall for some of its length In many people the colon is even more responsive to the emotional state than is the stomach. Spasticity of the descending colon is sometimes easily felt by palpation and may be demonstrated in most instances by the barium enema. It may occur transiently in association with acute emotional upheavals, or it may be present more permanently in some of the prolonged psychiatric disorders In contrast with peptic ulcer, outspoken psychiatric disturbances are the rule rather than the exception in spasticity of the colon and in mucous and ulcerative colitis. Many of the patients with ulcerative colitis are persons who have always reached out after an impossibly high degree of security; they are reserved and self-centered and most reverend toward any involved ritual. This is also true of mucous colitis which some regard as a precursor of the ulcerative type. An uncomfortably high percentage of patients with ulcerative colitis succumb to their disease, and many of these deaths are properly regarded as lethal complications of a neurosis. Usually by the time ulcerations of the colon have occurred the psychiatric symptoms are beyond effective therapy for either condition. In many patients the ebbing and flowing of anxiety is mirrored by alternating periods of constipation and diarrhea. The diarrhea of extreme fright is proverbial.

The *bladder* is an organ little subject to anatomic changes as a sequel to long continued emotional disturbance However, symptoms of urgency, fre-

A bladder symptom which is traditionally linked with emotional problems is enuresis. Most children learn adequate bladder control by the time they

lated in such cases that there was intermittent excessive constriction of the coronary arteries because of autonomic imbalance in response to anxiety situation. Ordinarily patients who contract coronary artery disease, and who have not had any previous history of *noteworthy anxiety, do not* exhibit any undue concern between attacks. It is not safe to depend solely upon this generalization as a diagnostic criterion, however.

The patient's realization of the presence of extrasystoles may be a source of more concern to him than to his doctor. The same is true of idiopathic or paroxysmal auricular fibrillation. Many patients who are told after examination that they are free from cardiac disease are not concerned any longer about it, but in some patients old anxieties which have lain dormant many years are reawakened and precipitated by precordial symptoms of pain or palpitation into a full-blown neurotic syndrome. In spite of reassurance anxiety is, of course, augmented by the popular fears concerning cardiac disease and sudden death as well as by well intentioned, but ill-advised "enlightening" publicity. In many of these the threat of impending dissolution persists long after the disturbance of cardiac rhythm has disappeared.

Abdomen

The abdomen contains many structures the functions of which are strongly tied to the mental life. This tie is exerted through the faster acting autonomic nervous system and the somewhat slower acting endocrine apparatus. If, for the purpose of this discussion, the endocrine glands are regarded as an extension of the autonomic nervous system, no great violence will be done to scientific exactness. The most responsive of the abdominal organs from the standpoint of direct symptoms are the stomach, the colon, and the bladder.

A large number of patients come to physicians in their offices and in clinics with complaints of "indigestion, gas, can't belch, food incompatibility, sour eructation, and can't eat." The majority of these patients show no anatomic and very little functional deviation from the normal on extensive investigation of the stomach involving physical examination and history taking, roentgen studies, gastric analysis, and gastroscopic examination. The ***diagnosis of a mental syndrome in these patients should never be made on the basis of negative physical and laboratory findings alone.*** Some of these patients whose diseases at first cannot be diagnosed, later turn up with sufficient objective evidence to warrant naming some anatomic change as the responsible agent. The diagnosis of a mental syndrome in these patients (or any others with somatic complaints) must depend on the psychiatric evidence alone, whether or not there is, in addition, some anatomic disease. Many authors, notably since the time of Charles Darwin, have commented on the response of the stomach to emotional changes. If these emotional changes be present long enough, or frequently enough, what then may happen to the structure of the stomach?

Many authors have argued that peptic ulcers, either of the stomach or of the duodenum, are a natural sequel to the effects of repeated or long [illegible] Examination from the psychiatric standpoint of [illegible]

In dealing with psychiatric problems in women, a woman office assistant should be at hand to forestall any subsequent unpleasantness the patient's disturbed mentality may create. Some women who have been overtly homosexual may be embarrassed by the presence of another woman.

In problems of adolescence and puberty the doctor's examination of the genitalia often inferentially helps the developing child to place his fears and doubts about sex in proper perspective. Care should be taken to place no undue stress on this part of the examination and so destroy its therapeutic value.

Extremities

The hands of a patient often tell stories about the mold in which he is cast. The nail biters are seldom well adjusted. Patients with hands that show the calluses of toil are less apt to be unnecessarily concerned about the question of health. The patient who comes to the doctor's office with painted finger and toenails has obviously the leisure and the vanity to care [illegible]

mental unrest which is expressed partly in chain smoking of cigarettes Cold hands and feet may be the expression of an imbalance of the autonomic nervous system in response to psychiatric problems. On the other hand, warm, sweating hands coupled with an anxious look and rapid pulse form a triad of hyperthyroid symptoms which demands further investigation. Raynaud's disease of the fingers or toes in mentally disturbed people brings to mind the possibility of a similar trophoneurotic disturbance elsewhere, even within the nervous system itself The trophoneuroses are poorly understood, but many cases respond moderately well to psychotherapy where other measures fail.

Body Build

In the past, particularly under the influence of Kretschmer, a great deal of attention has been paid to the relation of body build and other anthropologic features to psychiatric disorders. Some mentally deficient people do have certain features which seem to be associated with stupidity and reversion to the anthropoid primate type of body build This association is of very little importance practically, since no great clinical dependence on these features is warranted. The schizoid psychoses are said to occur mainly in people with poorly developed, immature types of body build. The manic on the other hand is said to be of the heavy, athletic build. These points do not easily lend themselves to clinical usefulness The body build is determined and modified, at least in part, by the functions of the endocrine system. In turn, the glands of the endocrine system are influenced by the autonomic nervous system and the latter responds to the emotional state. At that point the circle is completed for the emotional state can also be influenced by endocrine activity While all this appears to be as true as generalizations can be, the fact remains that sufficient information has not yet been accumulated to make clinically useful this indicated, but largely unexplored, field In certain specific situations such as acromegaly and giantism in which psychiatric syndromes may sometimes exist, the body build may be an important feature, however.

reach their first or second year of life. Some persist in enuretic disorder until late in childhood or even into adult life. The presence of adult enuresis is not in itself proof of the existence of a psychiatric disorder, nor is it necessarily to be regarded as some sort of epileptic equivalent. Congenital defects and neurologic disease may be responsible for some few cases of enuresis, faulty habit formation and training may be responsible for others, and still more cases show a demonstrable connection with a psychiatric disorder, but a great many cases have no known cause at all. Fortunately few cases of enuresis persist past puberty.

The possibility of mental symptoms arising out of primary disease of the abdominal organs merits at least a suspicion in many instances. The malignancies of the stomach, rectum, prostate, and uterus, and to a lesser extent those of the colon, adrenal glands, pancreas, and retroperitoneal structures may all give rise to brain metastases. As a rule in such situations the mental symptoms, if they are present at all, are a minor part of the total symptom complex. More important in our considerations are the chronic infections of the prostate, uterus, and appendix. Many cases of non-specified encephalitis have responded well to the removal of such foci of infection. Neurotic symptoms may be favorably influenced by such treatment, as they may be by any therapeutic measure which has a high enough suggestive value. This is a matter difficult to evaluate. Non-malignant, non-diabetic disease of the pancreas may begin with marked anxiety as the earliest and most prominent feature This is a rare situation, but interesting to the doctor whose index of suspicion is high.

Genitalia

Examination of the genitalia is an integral part of the psychiatric examination There are several reasons for this. It may give information as to the past or present existence of venereal disease Not infrequently one may find indications of self mutilation which may help the doctor in his psychiatric estimation of the patient. Among these are the enlarged labia minora frequently seen as a result of repeated masturbation in females; tattoos, particularly on the head of the penis*; lacerations and others. Precocious sexual development is easy to see in the male, although it is more difficult to ascertain in the female. It may have little psychiatric significance, but it is often associated with precocious sexual behavior. It occurs in tumors of the pineal, pituitary, and adrenal glands, and with other endocrine disturbances. The fact of virginity or the lack of it may be noted in females. In children poor personal hygiene may be a very important factor in the milder behavior disorders, as chronic irritation of the genitalia may draw a disproportionate amount of attention to these parts. Another important reason for never omitting the examination of the genitalia is to convey tacitly to the patient that the genital regions are neither less nor more important than are other parts of the body, and that his problems are being viewed from all angles. The patient often appreciates this attitude more than he may be embarrassed by the invasion of his privacy. His later reflections on the thoroughness of the examination far overbalance any momentary doubts.

* One of the most interesting was a tattoo of a bee with its stinger pointing toward the

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Measurements

Many varieties of physical measurements of the rate of recurring functions (such as respiration) or the cytology, immunology or chemistry of the body fluids may severally be indicated in individual patients. One of these, the examination of the blood for serologic evidence of the presence of syphilis, should never be omitted.

SUMMARY

This chapter has attempted to indicate the important points of the physical examination in patients who have psychiatric symptoms. There are no limits to the extent of the examinations which may be carried out other than the practical ones of time and expense. Ordinarily, it is best for the laboratory examinations to be less, rather than more, extensive, as patients with somatic conversion symptoms tend to overvalue the ominous importance of their symptoms because of multiple negative laboratory reports, and in extensive laboratory work they may sense a justification of their anxieties.